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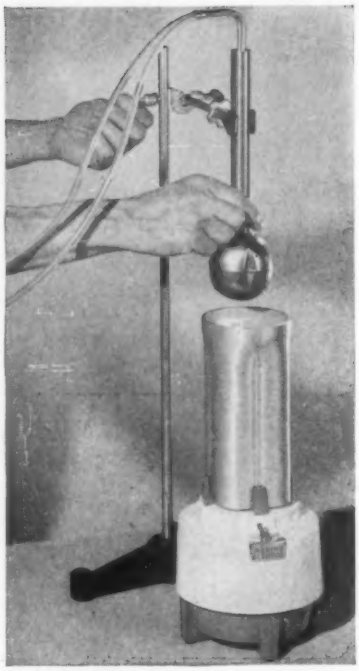

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International Symposium on the Dynamics of Virus Infections

Frank L. Horsfall, Jr.

Hospital of The Rockefeller Institute for Medical Research, New York

AN International Symposium on the Dynamics of Virus Infections, under the auspices of the Henry Ford Hospital, was held Oct. 21-23, 1953, in Detroit, Michigan. It was the first of an annual series on medical subjects planned by the staff of the Henry Ford Hospital.

More than 400 physicians and investigators attended the three-day conference which took place in the remarkably well-appointed new auditorium of the Henry Ford Hospital. Thirty-three investigators were invited to present papers. Six scientists who gave papers came from countries other than the United States.

Workers in the three major categories of the virus field—animal, bacterial, and plant—presented the results of their recent studies bearing on the following general subjects: (1) Mechanisms of virus and rickettsial infections, (2) Ecology and pathogenesis, (3) Mechanisms of immunity, (4) Methods of virus and rickettsial diagnosis, and (5) Chemical approaches to prophylaxis and therapy of virus and rickettsial diseases. No attempt is made here to summarize all the findings reported or all the concepts put forward. The communications as well as the discussions which followed them are to be published in full by Blakiston Company, Inc.

It was obvious during the symposium that much attention is being given to the mechanism of virus reproduction and that this problem is one of the foremost in the animal, bacterial, and plant virus fields. The approaches are diverse and include studies on surface interactions, cell penetration, metabolic transformations, continuity of virus characters, composition of viruses, and by-products of reproduction.

A surface reactant for the influenza-Newcastle-mumps group, consisting of a carbohydrate complex containing four sugars and carboxy-pyrrole, has been identified, and is thought to represent the small prosthetic group of large mucoproteins which react with these viruses. That the same substance is present at the surface of infectable host cells remains to be demonstrated directly.

The attachment of phages (T series) to *E. coli* has been found to be dependent upon electrolytes and appears to be attributable to linkages between bacterial surface carboxyl groups and phage amino groups. This interaction is reversible. Electrostatic triggering then is thought to modify both the cell surface and the phage particle so that penetration of phage DNA can occur. This step is irreversible. Two distinct processes appear to be initiated by phage; the reproductive process resulting in the production of new phage, and the lytic process leading to disorganization of the host cell. Under conditions that lead to so-called abortive infection—infection not resulting in infective progeny—these processes can be separated.

A new pyrimidine, 5-hydroxy methyl cytosine, is present in the virus nucleic acid of the T even phages. This is not a metabolic intermediate normally present in the host cell. It is thought that the infecting phage particle may provide the necessary enzyme or coenzyme, or possibly evoke a bacterial enzyme not normally used. In addition, in thymineless *E. coli* mutants, infection with T2 phage results in the synthesis of both thymine and 5-hydroxy methyl cytosine. Thus, in this instance, the only pyrimidines synthesized are those that the uninfected host cell cannot make.

Phage DNA is thought to start off infection with T2, and only a few molecules per bacterium are needed. The bacterial DNA appears to be efficiently used in the production of new phage DNA. The precursors of infective phage particles, so-called vegetative or noninfective particles, multiply, interact, and presumably contain the same nucleic acids as the mature particles. Phage protein appears to have no function during replication and is thought to be synthesized later than phage nucleic acid. DNA is considered to be the sole agent of genetic continuity in phage.

The formation of both the head and the tail antigens of phage precedes the production of mature particles. Both antigens arise during the multiplication of vegetative phage. Maturation—the completion of mature, infective particles—appears to be a stepwise process; the synthesis of the specific phage materials, that is, DNA and proteins, precedes the less specific assembly of the mature particle.

The reproduction of tobacco mosaic virus is preceded by an increase in the insoluble nucleoprotein of the host tissue. It is thought that this is related to the formation of cell particulates which are the site of synthesis of virus protein. Such protein then is associated with accumulated virus RNA to yield mature virus particles. TMV reproduction is accompanied by the synthesis of three new low molecular weight (*ca* 30,000) proteins not associated with nucleic acids. The new proteins appear later than the virus, when the excess nucleic acid has disappeared; they are serologically related to TMV and can be polymerized. With plant viruses, in sharp contrast to bacterial viruses, genetic information apparently cannot be transmitted by DNA, for none is present. Whether RNA carries out such a function for plant viruses remains to be shown.

All stages of plant virus infection seem to be affected by the metabolism of the host cells. Both susceptibility and the amount of virus formed are increased by nutrients that increase plant growth. Susceptibility and virus multiplication can be affected separately by some chemical substances; however, thiouracil decreases both and is most effective when plant metabolism is high and would normally support most virus reproduction. Virus disease in plants is thought to result from aberrations in host protein metabolism.

The metabolic transformations associated with the reproduction of animal viruses remain largely unexplored. In addition, there is as yet no definite evidence on the nature of the material that transmits genetic information for these agents. The difficulty of demonstrating a possible transfer of genetic material between animal viruses remains largely unresolved. However, with influenza viruses the results of double infection experiments indicate that phenotypic mixing may occur and that a state analogous to heterozygosis can develop. It appears that single particles can carry the potentiality of giving rise to particles corresponding to both parental types. With influenza viruses, earlier indications of genetic recombination seem now to be best explained on the basis of phenotypic mixing. Similar transient alterations in the phenotype also have been demonstrated with certain T phages.

Animal virus reproduction appears to be associated with the production of new proteins separable from the virus particle, for example, soluble complement fixing antigens. In addition, there is evidence that noninfective, or "incomplete," influenza virus particles may appear in high yield under unusual experimental conditions with very large inocula. Except that they lack the highly unstable property of infectivity, such particles appear not to be markedly different from fully active particles. It has yet to be shown decisively that immature particles, comparable to those obtained with phage, are necessary precursors in the reproduction of animal viruses. Relative to cellular structures, mitochondria are thought to represent the intracellular sites of multiplication of herpes virus, possibly also of poliomyelitis virus, and may play a similar role with rabies virus.

Virus infection and bacterial transformation have as common features an invasive and replicative series of events. Each of the individual DNA transformers can be considered as an independent agent capable of invading, producing a modified bacterial cell, and being reproduced like a virus. In addition, DNA-induced transformations are closely analogous to genetic mutations, with the difference that they are directed. The stepwise transformation to drug resistance achieved with DNA appears to correspond exactly to the series of spontaneous mutations undergone by the donor strain during the acquisition of resistance.

The importance of reservoir hosts in the ecology of certain animal virus diseases—bovine pseudorabies, salmon poisoning, and swine influenza—appears to be well established. Such hosts determine the endemicity of these infections. In virus diseases of man, there is only incomplete knowledge of the whole ecological cycle in most instances. The sites at which viruses leave an infected host, as well as the means by which the agents are transmitted to and enter new hosts, are widely diverse. The role of the immune host in the transmission chain seems to be variable. As an example, it appears that measles and chicken pox do not have healthy carriers, but it is thought that infectious hepatitis and poliomyelitis may.

Population fluctuations of pathogenic agents, reservoirs, vectors, and hosts are affected by deforestation and human settlement. These fluctuations encourage evolutionary adaptation, especially evident in the genus *Rattus* and among *Trombiculid* mites in Southeast Asia, and bear on the ecology of scrub typhus. In the plant virus field, it has been demonstrated that the leaf-hopper is not only an efficient transmitter of aster yellows virus but it also is a superb reservoir for this agent. In the main, the vector remains infective throughout its life.

In poliomyelitis, there is uncertainty as to the common route by which the virus migrates from the alimentary tract to the central nervous system. There appears to be no doubt that the agent can reach lymphatic organs, enter the blood stream, and travel along nerve fibers. It is clear that the virus can multiply in the alimentary tract, the CNS, and possibly also in lymphatic tissue. The function of immune barriers in poliomyelitis seems to depend on the hypothesis favored for transmission of the virus from the periphery to the CNS.

Inapparent natural infections are thought to lead to as effective immunity to virus diseases in man and animals as recovery from manifest infections. Infective virus vaccines, prepared from variant strains, appear to mimic inapparent infections and may induce substantial immunity. Widespread application of such vaccines, excluding those against smallpox and yellow fever, has been prevented by the difficulty of securing and maintaining appropriately avirulent variants, as well as the potential hazard of causing frank disease. To induce immunity, it appears that the variant virus in an infective vaccine must multiply in the tissues of the vaccinated host. That such agents do not cause obvious disease is correlated with the finding that the rate of increase in virus concentration as well as the final yield of virus are lower than with virulent strains.

Inactivated virus vaccines, although incapable of causing infectious disease if actually free of infectious agents, are not without disadvantages. A relatively large amount of antigenic material is needed to give a satisfactory immune response and, in the absence of an adjuvant, this may be of short duration. Repeated injections may lead, if considerable foreign tissue material is present, to hyperreactive states.

The problem of early diagnosis of virus diseases of man has been solved in relatively few instances. Smallpox remains the best example and a specific diagnosis can be made rapidly through detection of the virus

antigen by *in vitro* procedures. For other viruses and rickettsiae, there are not yet available simple and reliable technics for the detection of specific antigens early in the disease process. Recovery and identification of the infectious agent and the demonstration of a specific antibody response after the early stages of the disease constitute the mainstays of laboratory diagnosis. Both have the disadvantages of requiring considerable effort and time and therefore tend to yield information only of retrospective value. Recent advances in tissue culture methods have simplified the diagnostic problem in some virus diseases, particularly in poliomyelitis. In this disease, tissue culture has largely replaced the experimental animal as a means for recovery and identification of the virus and measurement of specific antibodies. In addition, the newer tissue culture technics have made feasible the propagation of varicella and herpes zoster viruses, possibly also common cold virus, and have resulted in the recovery of a number of seemingly new infectious agents.

Although effective chemotherapeutic agents are now available for all rickettsial diseases and for those diseases caused by the psittacosis-lymphogranuloma venereum group of agents, there is still no good evidence that substances, useful in man, have been found for other virus infections. However, vigorous efforts in this direction continue and some substances capable of inhibiting the reproduction of certain animal, bacterial, or plant viruses under experimental conditions are now known. The effects of proflavine on phage multiplication appear to be best understood. The compound is thought to prevent the final assembly of the mature virus particle but does not affect the earlier production of either phage proteins or nucleic acid. However, despite its effect upon the bacterial virus, proflavine fails to provide any benefit to the infected bacterial host which proceeds to die at the expected time. Inhibitors of plant virus multiplication have received relatively little detailed study, partly because of technical difficulties, and it is doubtful that the effects of any can yet be described in mechanistic terms. In the animal virus field a variety of substances of widely dissimilar nature have been investigated intensively but only in a few instances, for example, with mumps and influenza viruses, have kinetic studies on inhibitor activity been undertaken. Chief interest appears to be in compounds that may act as inhibitors of required biosynthetic processes. Various so-called antimetabolites such as analogues of amino acids and derivatives of benzimidazole, cause effects in some virus infections that may prove to be of importance.

The Radioactivity of the Human Being

A. T. Krebs

Army Medical Research Laboratory, Fort Knox, Kentucky

THE amount of radioactive substances deposited naturally in the normal human being has become one of the key figures in recent discussions on "tolerance" dose, "permissible" dose and "damaging" dose in repeated, as well as in single, total body exposures to ionizing radiations. Its magnitude, originally reported by Krebs (*1–3*) as close to the accepted permissible body content of 1×10^{-7} gram radium element permanently fixed in the body, became uncertain, when Hursh and Gates (*4*), in 1950, found values 100 to 1000 times smaller than the accepted permissible content. While the reasons for this discrepancy were under discussion, Sievert (*5*), in 1951, using a special gamma-ray sensitive device for measurements on the intact living body as a whole, reported an average radioactivity of the human being close to the values given by Krebs and, thus, close to the permissible content. In connection with present considerations on the extension to man of the findings from experimental whole body irradiation studies (*6*), a critical review of the present situation seems adequate in order to come to an understanding of the reported values.

The data on total body radioactivity of the human being so far reported are presented in Fig. 1. They were obtained by Krebs in the study of 17 cases in the age range 50 to 91 yr, by Hursh and Gates in 25 cases in the age range 33 to 85 yr, and by Sievert in 12 cases in the age range 15 to 58 yr. Krebs measured his samples with an especially developed alpha-particle counter and with the emanation method. His values are given in amounts of radioactive substance equivalent to radium and/or radium element. Hursh and Gates used exclusively the emanation method and reported their findings in radium element. Sievert measured the radioactivity of the living individual with

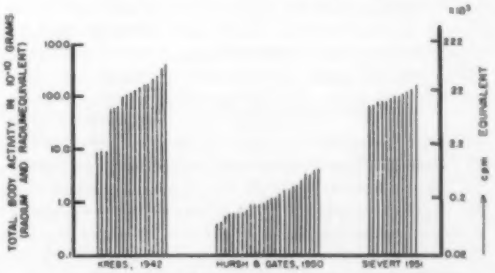

FIG. 1. Radioactivity of the normal human being.

TABLE 1. Radioactivity of tissue from uranium miners (St. Joachimsthal) (Behounek and Fort, 1941).

Age of miner (in yr)	Activity per gram of fresh tissue (in 10^{-12} g)			
	Emanation method*		Alpha activity method†	
	Lung	Vertebra	Lung	Vertebra
34	9.7	533	316	432
37	13.5	290	256	518
40	12.7	403	154	109
44	3.5	312	27	210
46	8.5	377	71	410
46	8.2	290	71	660
49	15.0	460	22	50
50	5.8	534	22	395
62	10.3	367	174	315

* Records only radium element.
† Records all alpha emitting radioactive substances.

special gamma-ray sensitive ionization chambers. His values are presented in gamma radium equivalent, which means in amounts of radioactive substance the magnitude of which is equivalent to the gamma radiation emitted by the proper amount of radium element. In evaluating and comparing, with these facts in mind, the presented data, the question immediately arises regarding the principles and the characteristics of the different methods used for the determination of the activities.

The normal emanation method, one of the most outstanding procedures in classical radioactivity studies, measures the amount of radium element in the sample. It does not detect other possibly present, nonemanating radioactive substances. Even short-lived emanations, such as thoron with a half-life of about 54 sec, which indicate the presence of active compounds, can be measured only with specially constructed experimental attachments. Thus, it already becomes evident that the particular method used determines the type and the amount of radioactive material that will be reported.

The methods based on gamma-radiation measurements record the activities of practically all gamma-ray emitting elements in the tissue and in the body, independent of location and distribution. The values obtained with these methods will always be higher than the pure radium element values, since man incorporates from his environment into his body not only radium but also other gamma-ray emitting radioactive substances. Since Sievert's device measures the activity of the living body as a whole, it offers another great advantage in comparison with methods that measure only the activity of certain tissue and body parts and require calculation of the total body activity

TABLE 2. Radioactivity of the human being.

1. Total body radioactivity

a. Normal cases

Investigator	No. of cases	Age (yr)	Activity range (in 10^{-10} g)	Average activity (in 10^{-10} g)
Hursh and Gates, 1950	25	33–85	.38–4.3*	1.5*
Sievert, 1951	12	15–58	67–165†	103†
Krebs, 1942	18	50–91	10–400†	140†

b. Occupationally exposed cases

Sievert, 1951	12	25–64	90–680†	

* Radium element
† Radium equivalent

2. Tissue radioactivity

a. Normal cases

Investigator	Tissue	No. of cases	Age (yr)	Activity in 10^{-12} g radium equivalent
Krebs, 1939/42	Muscle	6	47–88	10– 300
	Lung	9	18–88	60– 6500
	Vertebra	5	47–75	700– 4600

b. Occupationally exposed cases

Krebs, 1942	Lung	17	38–68	20– 9000
Behounek and Fort, 1941	Lung	21	34–62	225– 5550
	Vertebra	10	34–62	500–20,000

3. Natural radioactivity of body, after Grosse and Libby (*5*)

Element	Potassium	Carbon	Radium	
Amount per body (in g)	280	14,400	8×10^{-9}	4×10^{-9}
Nature of emitted particle	Beta	Beta	Alpha	Alpha
cpm from total amount	380,000	150,000	18,000	9000
Reference	Sherman	Sherman	Vernadsky	Evans, R. D.

by multiplying the tissue activities with estimated tissue and organ weights.

The investigations based on particle counting and particle ionization measuring methods will give values close to the upper limits of the radioactivity of the body. These methods record especially all alpha-particle emitting elements accumulated in the body under the individually given conditions. They include the main radioactive elements and their decay products, the uranium, thorium, and actinium families. These values should contribute decisively to the picture of the internal irradiation burden to which man is subjected.

There is a definite difference between the amount of radium and the amount of radioactive substances to be found in tissue, as may be seen from the values obtained by Behounek and Fort (*7*), when measuring one and the same tissue with two different methods (Table 1). There is however, no consistency in the ratio of these two values. The ratio of radium content to radioactive-material content changes from case to case, depending on the history of the case and on the physiological state of the individual as well as on the rate of accumulation and excretion for the individual radioactive element in the body.

It should be kept in mind, therefore, in any discussion of the problem that the emanation method gives the amount of radium element present in the body; the gamma-ray sensitive methods measure the activity in gamma radium equivalent; and the alpha sensitive methods preferentially record the radioactivity of the body in alpha radium equivalent. In the earlier publications on the radioactivity of normal and abnormal tissue, this was clearly stated and emphasized; later and even in recent publications this distinction was lost in the discussion of details.

Application of these criteria to the radioactivity values presented in Table 2 leads, therefore, to the following conclusions. Measurements of the radioactivity of the human body with methods that record radium element *per se* show, in general, the lowest values. Measurements with particle-counting devices and/or with alpha and gamma radiation sensitive ionization setups give higher values, since these methods record, besides radium element, other radioactive substances that are accumulated and deposited in the body from its environment during the years.

There is no definite, discrete value of the radioactivity of the human being. Like all other biological values, this value also covers a range rather than showing one proper figure (*9*). The amounts of radium element to be found in the body seem to be well below the accepted permissible radium content of 1×10^{-7} *g* per body. The amounts of radioactive substances deposited in the body, however, exercise an irradiation burden on the body close to the accepted tolerance figures. They are, nevertheless, much lower than the toxic amounts found so far in radium-poisoning cases. The question, insofar as these findings and the knowledge gained in radium-poisoning cases can be extended to total body irradiation studies on man, by applying the time-intensity law, requires special considerations.

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News and Notes

Entomologists Meet

THE 1953 Annual Meeting of the Entomological Society of America was held at the Hotel Biltmore, Los Angeles, Calif., Dec. 7–10, 1953, with nearly 700 entomologists registered. The president for 1954, Dr. H. H. Ross of the Illinois Natural History Survey, was installed, and the election of Dr. George C. Decker, of the same organization, as president-elect was announced. The next Annual Meeting will be held at Houston, Tex., Dec. 6–9, 1954.

The recent meeting was the first since the Society's reorganization resulting from the consolidation of the American Association of Economic Entomologists (1889–1952) and the former Entomological Society of America (1906–1952). Dr. E. G. Linsley, of the University of California, Berkeley, spoke on the role of taxonomy in the new Society and predicted that increased encouragement for taxonomic studies could be expected. The great value of taxonomic work was one of the views also stressed by Dr. C. E. Palm, of Cornell University, the retiring president, in his address, "The growing responsibility of entomology to human welfare." A concluding thought of his address was expressed in his appraisal of the future progress of entomology as a profession: "The key to future gains, and our ability to serve, lie in the support and conduct of basic research in broadest terms for all aspects of entomology. The entomologist can no longer withdraw from his obligation to share his knowledge about insects with the public who must be informed if it is to support him adequately."

The resistance of insects to insecticides was discussed by several speakers, including Dr. Palm, who in his address suggested that the occurrence of resistant strains of insects may well be responsible for the growing support of basic physiological research, which despite its importance has been neglected too often in the past. Drs. R. B. March, R. L. Metcalf, and L. L. Lewallen, of the University of California

Citrus Experiment Station, Riverside, presented their opinions of resistance, based on the lessons of five years experience with house flies. They pointed out the limits of resistance and reasons for a moderate feeling of optimism regarding this baffling problem.

The Annual Invitational Public Address was given by Dr. Herman T. Speith, head of the Department of Biology, University of California at Riverside. His topic was "Relation of Drosophilid mating behavior to population structure." He described the quite different mating habits of various closely related fruit flies and explained their significance in contributing to the distinctness of species. One of the most thought-provoking talks, among the more than 175 presented, was that of Dr. G. C. Decker, "The role of insects in the economic future of men." His remarks left no doubt that insect problems will continue to be with us, regardless of present synthetic insecticides.

One of the newer approaches to the control of insects parasites of livestock was outlined by Drs. W. S. McGregor and R. D. Radeleff, of the U.S. Department of Agriculture, Kerrville, Tex. They described tests made by giving subcutaneous injections of insecticides dissolved in peanut oil to guinea pigs, which later demonstrated that some protection was afforded by certain of the chemicals when the animals were artificially infested with screw-worm larvae. This method of injecting host animals with insecticides is being tested experimentally with cattle, in relation to such pests as cattle grubs, ticks, stable flies, and horn flies.

There was a special seminar on "The use of photography in entomology," in which five California entomologists participated. Both equipment and outstanding results were demonstrated.

The new business office of the Society is located at 1530 P St., NW, Washington 5, D.C.

ASHLEY B. GURNEY

Executive Secretary

Science News

On Mar. 17 the President of the United States issued an Executive Order designed to strengthen the conduct and administration of the scientific research and development programs of the various departments and agencies of the Federal Government. The order directs the National Science Foundation to make studies of the scientific activities of the Nation and to recommend to the President policies to strengthen the research effort and define the Federal Government's role in it. The Foundation, over a period of time, is expected to become increasingly responsible for providing Federal support for basic research carried on in universities and other nonprofit institutions. Other Federal agencies, however, will continue to carry on basic research which is closely related to their statutory missions. The Foundation will also study the effects of Federal research support on the Nation's educational institutions and recommend policies and procedures to promote the attainment of the Federal research objectives while safeguarding the strength and independence of the educational institutions.

The order also directs the head of each agency engaged in research to make sure that such programs reflect urgent needs and are carried on economically and with regard to the efficient use of scientific manpower. In this connection the order provides a new method to facilitate the exchange of scientific equipment and facilities among the Federal agencies so as to avoid buying new equipment or building new facilities when another agency has unused equipment or facilities available. In connection with his approval of the order, the President made the following statement:

> Science has a vital role in our Nation's security and growth. During the past half-century, it has brought about a vast transformation in industry, in agriculture, in medicine, in transportation, and in communications. Military science has been revolutionized by technological development. The impact of science is increasingly felt in every field of public policy including foreign affairs. All this has been brought about through a combination of vision, initiative, business enterprise, a strong educational system, and the dedicated enthusiasm of the scientific community.
>
> The responsibilities of the Federal Government toward science have likewise changed greatly. In 1940, the Federal Government spent about one hundred million dollars in supporting research and development. The budget which I have just transmitted to the Congress calls for expenditures for these purposes in the next fiscal year of over two billion dollars. This is convincing evidence of the important role of science and technology in our national affairs.
>
> This rapid expansion of Federal responsibility requires prudent administration. More than half of all the investment in the Nation today for scientific research and development is being made by the Federal Government. In large measure, these Federal funds are paid to industry and educational institutions for the conduct of research and development projects. Thus our Federal policies and practices regarding research and development are felt immediately and substantially by industry and our educational institutions.
>
> More than 90 percent of this Federal support is presently going into applied research and development. This is the practical application of basic knowledge to a variety of products and devices. However, only a small fraction of the Federal funds is being used to stimulate and support the vital basic research which makes possible our practical scientific progress. I believe strongly that this Nation must extend its support of research in basic science.
>
> While the Executive Order which I have signed today calls upon the National Science Foundation to carry out important responsibilities in regard to scientific research, it is also designed to strengthen the conduct and support of vital research and development in the several agencies where science is important in achieving their assigned missions.

This order will, for the first time, set in motion important steps leading to a thorough and continuing review of the status of the Federal Government's activities in science, and thus enable the Government, together with industry, higher education, and the scientific community to move forward with assurance toward the achievement of the Nation's goals.

I expect and believe that this order will clarify the position of the Government toward the support and advancement of science in the Nation, and that it will contribute in a constructive sense to the development of our national policy in this important and critical area.

Britain's Ministry of Supply has revealed the existence of a new industry in the United Kingdom, an industry developed on schedule in face of formidable technical and economic difficulties. In a foreword to **"Britain's Atomic Factories,"** a government publication, Mr. Duncan Sandys, British Supply Minister, says "It is right that the world should be told how fissile material is today being produced in Britain and of the remarkable factories and plant which have been designed and erected to carry out these strange processes." Center of this enterprise is Risley, Lancashire. Here were evolved blueprints for three large factories at Springfields, Windscale, and Capenhurst in the British North West. What Britain's Harwell center is to atomic research, Risley has become to atomic production. Risley began operations in February 1946 with a total strength of 12 men and women, and "of this group only one man knew anything at all about atomic energy."

Windscale, the plutonium plant, is now producing in quantity from its two piles material equally vital for power in war or peace. The chimneys of the pile tower over 400 ft above the landscape, and the factory space occupies some 300 acres and is staffed by nearly 5000 men, including over 300 architects, engineers and surveyors. Special traps and filters render the cooling air harmless before it passes out of the stacks; press-button operated shut-down rods, steel-lined concrete walls several feet thick, and warning devices make work on the piles safer than in a toy factory. So good are safety precautions that a worker who obeys the rules including wearing of special clothing, "has no chance of coming to harm in 30 or 40 years of work." That atomic production has become one of the safest of trades is largely due to emphasis on health measures by the British and development of super-sensitive instruments to "smell-out" radioactive contamination. Eating and smoking are prohibited in active areas, and all personnel must wash before leaving the job.

Typical of the immense difficulties overcome by the Risley organization is the disposal of radioactive effluents in cooling water from the Windscale plant. To achieve this safety two pipes, each 1 ft in diameter and 2 mi long, had to be laid on the sea bed within a strict time limit imposed by the tide; this operation was accomplished by welding the pipes into ½-mi lengths and towing them out to sea.

Driving force in the British atomic energy production program is Sir Christopher Hinton, a distinguished engineer loaned from industry to arms production in the war.

No country needs this development more than Britain, whose coal requirements for electricity production are likely to increase by 63 million tons in the next 15 yr. And Britain is struggling to maintain coal output, even at existing inadequate levels. If and when the heat from the Windscale plutonium piles can be used economically to generate electric power, Britain's economic position could be transformed. What "might possibly be realized within 20 years," says Mr. Jay, "would be to set up a reactor system which would generate enough electricity to produce a saving of 20 million tons of coal a year, the amount by which estimated production will fall short of estimated consumption during the next 15–20 years." As a start, recalls Mr. Jay in his report, "Minister of Supply Duncan Sandys announced to the House of Commons on April 30 this year that work would start on an experimental atomic power station adjoining the Windscale plant "in a few days' time." This station, when completed, will probably be "the first of its kind in the world."

World Health Day is the anniversary of the coming into force, on Apr. 7, 1948, of the Constitution of the World Health Organization. The observance of this date affords an opportunity to help arouse throughout the world popular interest in health needs and to stimulate the people's participation in the task of improving health.

Scientists in the News

Roland H. Berg, for the past 10 yr director of scientific information for the National Foundation for Infantile Paralysis, has joined the editorial staff of *Look* magazine as medical editor.

Elmer K. Bolton of Wilmington, Del., a leader in the development of nylon and in the synthesis of neoprene, first general purpose synthetic rubber, has been named 1954 winner of the Willard Gibbs Medal of the American Chemical Society's Chicago Section. Dr. Bolton retired in 1951 as chemical director of the Du Pont Company. The Gibbs award is one of the highest honors in American chemistry and is conferred annually on an outstanding chemist selected by a national jury.

Gordon B. Carson has assumed the deanship of the College of Engineering at Ohio State University. This position was formerly held by the late Charles E. MacQuigg.

G. Robert Coatney, head of the Chemotherapy Section of the Laboratory of Tropical Diseases at the National Institutes of Health, has been named the winner of the Darling Foundation prize for his out-

standing work on malaria research. Announcement of the award was by the Geneva office of the World Health Organization.

Donald E. Coles, a research fellow in aeronautics at the California Institute of Technology, has been named winner of the annual Lawrence Sperry Award by the Institute of the Aeronautical Sciences. Dr. Coles was cited for his experimental and theoretical contributions to the basic knowledge of turbulent skin friction and heat transfer at supersonic speeds.

In March friends of **Prof. Peter Debye** of the Cornell University Chemistry Department gathered for the Debye 70th Anniversary Symposium. Prof. Debye, who has continued in research since his retirement from teaching, was 70 on Mar. 24. He received a presentation copy of his collected works, which are being published this spring by Interscience Publishers.

James G. Horsfall, director of The Connecticut Agricultural Experiment Station, New Haven, has been granted a sabbatical leave which he will devote to research, teaching, and writing at the University of California, Berkeley. He will return to New Haven in July.

Lawrence C. Kolb, consultant in psychiatry at the Mayo Clinic and associate professor in psychiatry of the Mayo Foundation, Graduate School of Medicine, University of Minnesota, has been appointed director of the New York State Psychiatric Institute and professor of psychiatry and executive officer of the Department of Psychiatry, Columbia University College of Physicians and Surgeons. Dr. Kolb will also be director of psychiatry service at Presbyterian Hospital. All appointments become effective July 1. He succeeds Nolan D. C. Lewis, who retired from state service last September.

Frederick A. Mettler, professor of anatomy in the Department of Neurology, College of Physicians and Surgeons, delivered the annual Murray B. Gordon Memorial Lecture at the State University College of Medicine at New York City. The lectures have been given each year by original investigators who have made outstanding contributions to the advancement of medicine and its allied sciences. Dr. Mettler's special field of interest is diseases of the nervous system.

Seth Minot Milliken, surgeon and for 18 yr treasurer of the New York Academy of Medicine, received the Academy Plaque in recognition of his outstanding service to the Academy.

Charles C. Price has been appointed head of the Chemistry Department at the University of Notre Dame. Dr. Price served as head of the Chemistry Department from 1946 to 1952, but resigned the post to campaign as the Democratic nominee for U.S. Representative from Indiana's 3rd Congressional District. However, he continued to teach in the department.

Isadore S. Ravdin, professor of surgery at the University of Pennsylvania and surgeon-in-chief at the University's hospital, has received the Buffalo Surgical Society's Roswell Park Memorial Medal for "outstanding surgical achievement."

The Office of International Relations, National Academy of Sciences—National Research Council, has provided the following information concerning the travel plans of scientific **visitors to the United States:**

D. J. Griffiths, Welsh Plant Breeding Station, University College of Wales. Arrived in March for a 4-mo stay to study breeding techniques and their application to the breeding of oats in particular, on a Kellogg Foundation Scholarship. Will visit Iowa State College, University of Missouri, University of Wisconsin and other institutions.

D. M. Jackson, surgeon-in-charge of Medical Research Council's Industrial Injuries and Burns Research Unit, 38 Old Queen St., London. Here from Apr. 27 until mid-October for research work at the Massachusetts General Hospital in Boston (Dr. Oliver Cope).

Alexander King of the Department of Scientific and Industrial Research London, commenced 4-wk stay on Mar. 10. Is visiting research laboratories and government agencies to discuss problems relevant to work of the D.S.I.R. (United Kingdom Scientific Mission, Washington, D.C.)

W. C. Moore, director of the Plant Pathology Laboratory at Milton Road, Harpenden, Eng. (Ministry of Agriculture and Fisheries). Here Mar. 23–May 3 to discuss legislation, regulations, and quarantine concerning import and export of plants.

Rosalind Pitt-Rivers, National Institute for Medical Research, London. Arrived Sept. 1, 1953 for 1 yr of research in biochemistry at the Massachusetts General Hospital in Boston (Dr. R. L. Berg).

G. J. Popjack, Director, Medical Research Council's Experimental Radiopathology Research Unit, 38 Old Queen St., London. Here June 1–July 12.

Jarl Cecil Sarvas, Department Engineer, Electrical Inspectorate, Helsinki, Finland. Under auspices of the International Educational Exchange Service. Arrived Feb. 3 for 90 days. (Miss Elizabeth Jorzick, Programs Branch, Leaders Division, Department of State, Washington 25, D.C.)

A. W. Skempton of the Department of Civil Engineering at the City and Guilds College, South Kensington, Eng. Arrives in May. Will give lectures at the University of Colorado and elsewhere.

Macdonald Tow, Department of the Nuffield Professor of Surgery, University of Oxford, England. Arrived in January for several months. Fields of specialization are: functions of the frontal lobes; functions of cingulate gyri and orbital gyri in man; anatomical basis of intelligence, personality and emotions; long-term results of cingulate cortex and orbital cortex operations for psychoneuroses; long-term results of frontal lobe operations on social, spiritual and ethical

behavior in man. (Prof. Stanley Cobb, Massachusetts General Hospital, Boston 14.)

Peter Trench, Bovis Ltd., London. Here for about 4 wk from early April to May. Unofficial visit to study building methods and organization with a view to introducing in the United Kingdom such methods or organization that could help increase productivity and reduce building costs. (United Kingdom Scientific Mission, Washington, D.C.)

O. A. Trowell, Member of Medical Research Council's Radiobiological Research Unit, 38 Old Queen St., London. Here May 25–June 9 to attend conference New York on leukocytic functions. Various other visits.

Education

A new **course for secondary-school science teachers,** "Current Developments in Science," will be offered by the Harvard Summer School this year. A number of special fellowships are available for the course, which continues the series in Science Education initiated by James B. Conant, former president of Harvard. The course will last from July 6 to Aug. 18 and will carry 8 semester-hours' credit. It will be taught by Eugene G. Rochow, a professor in the Harvard Chemistry Department and a pioneer in silicone chemistry.

The course is designed to help teachers expand and strengthen their knowledge of basic concepts in the physical sciences, interpret new developments in these fields, and relate these developments and concepts to their own teaching. Current and recent work in chemistry, biochemistry, and physics will be discussed, and field trips will be made to nearby industrial and university laboratories. To make the course as valuable to teachers as possible, ways in which some of these topics can be used in high-school classes will be demonstrated.

Some of the fellowships will cover registration and tuition fees for the course; others will include the fees plus allowances toward room, board, and travel expenses. Awards will be based on qualifications, need, and geographic location of applicants. The course can be counted for credit toward the Ed.M. or the A.M. in teaching by those who are admitted to one of these degree programs in the Harvard Graduate School of Education.

Also of interest to teachers will be a number of courses in the sciences, including astronomy, biology, chemistry, physics, and mathematics, and a course on "The Philosophy of Science" by Max Black of Cornell University. Further information about these courses and the fellowships can be obtained from the Harvard Summer School, 2-N Weld Hall, Cambridge 38, Mass.

The Department of Neurosurgery, in conjunction with the Department of Physical Medicine and Rehabilitation, of New York University-Bellevue Medical Center has recently established a **peripheral nerve injury unit.** Thomas I. Hoen, professor and chairman of the Department of Neurosurgery, NYU Post-Graduate Medical School, and Howard A. Rusk, professor and chairman of the Department of Physical Medicine and Rehabilitation, NYU College of Medicine, are jointly directing the unit, which is in operation at the Institute of Physical Medicine and Rehabilitation, N.Y.

The Future Scientists of America Foundation has received a grant from the Crown Zellerbach Foundation to hold a **science teacher's summer conference** on Aug. 13–27. This venture in industry-education cooperation will bring a group of selected science teachers to Oregon State College to compare their high school science laboratory programs with the activities that are current in industrial, university, and governmental research laboratories. They will divide their time between using the facilities of the college and visiting research laboratories in Oregon and neighboring states. *Applications are being accepted any time before June 1* from all certified general science, physics, chemistry, and biology teachers in Arizona, California, Idaho, Nevada, Utah, and Washington. Each teacher will receive $200 toward the expenses of attending the conference.

Grants and Fellowships

The Philadelphia College of Pharmacy and Science is now offering to properly qualified students a number of **graduate assistantships in pharmacy** for the year 1954–55. These assistantships require 9 mo of service with a maximum teaching load of twelve student-contact hours weekly. Each assistant receives a stipend of $1000; tuition and all other fees are remitted.

Graduate assistants may enroll in curricula leading to the Master's or Doctor's degree in pharmacy, and may major in pharmacy, pharmacology, pharmaceutical chemistry, or biological sciences. A partial schedule of studies, approximating two-thirds the full-time assignment, may be carried. The assistant will require 2 yr to qualify for the Master's degree. For application forms and further information, write to the Secretary of the Graduate Committee at the College, 43rd Street, Kingsessing and Woodland Avenues, Philadelphia 4, Pa.

The **John and Mary R. Markle Foundation** has announced the appointment of the following 25 **Scholars in Medical Science,** all faculty members of medical schools in the United States and Canada, and the largest number to be appointed in any year since the Scholar program began in 1948. The fund has appropriated $750,000 toward the support of these doctors, to be granted at the rate of $6000 annually to the medical schools where they will teach and carry on research.

McGill University. J. C. Beck, Faculty of Medicine. Endocrinology and metabolism.

State University of New York. W. H. Bergstrom, Syracuse College of Medicine. Pediatrics and biochemistry.

University of Minnesota. G. S. Campbell, Medical School. Surgery and physiology

University of Manitoba. R. M. Cherniack, Faculty of Medicine. Internal medicine and pulmonary physiology.
Tulane University. W. H. Clark, Jr., School of Medicine. Pathology.
University of Washington. E. L. Foltz, School of Medicine. Neurosurgery and neurology.
University of Toronto. D. Fraser, Faculty of Medicine. Clinical pediatrics and physiology.
Duke University. W. E. Hull, School of Medicine. Physiology and pharmacology.
Johns Hopkins University. D. P. Jackson, School of Medicine. Clinical microscopy, especially hematology.
University of Cincinnati. J. B. Kahn, Jr., College of Medicine. Pharmacology and physiology.
Medical College of Virginia. R. Q. Marston. Internal medicine.
University of Oklahoma. W. T. Newsom, School of Medicine. Pediatrics and newborn and premature infants.
Queen's University. D. A. Rosen, Faculty of Medicine. Ophthalmology.
University of Vermont. R. H. Saunders, Jr., College of Medicine. Hematology and clinical pathology.
Howard University. M. W. Spellman, College of Medicine. General and cardiovascular surgery.
University of Missouri. H. E. Stephenson, Jr., School of Medicine. General and cardiovascular surgery.
Washington University. J. L. Strominger, School of Medicine. Pharmacology and biochemistry.
Harvard University. E. Suter, Medical School. Bacterial physiology, immunology, and infectious diseases.
Cornell University. R. C. Swan, Jr., Medical College. Physiology and internal medicine.
University of North Carolina. I. M. Taylor, School of Medicine. Internal medicine and physical diagnosis.
University of Rochester. S. M. Tenney, School of Medicine and Dentistry. Internal medicine and physiology.
University of Virginia. O. A. Thorup, Jr., Department of Medicine. Hematology and cardiology.
University of California. R. A. Ulstrom, School of Medicine. General pediatrics, pediatric endocrinology and metabolism.
Ohio State University. R. N. Watman, College of Medicine. General surgery and physiology.
Tufts College. C. W. Watson, Medical School. Neurology and neurophysiology.

The **University of Washington School of Fisheries** offers financial assistance to outstanding graduate students, undergraduate students, and high school seniors in the form of scholarships with awards from $250 to $500 per school year, and by assistantships and part-time employment with stipends ranging from $600 to $2000 per year. For further information address Dr. Richard Van Cleve, Director, School of Fisheries, University of Washington, Seattle 5, Washington.

Meetings and Elections

L'Aluminium Français and **La Société Chimique de France** will hold a scientific congress and exhibition in Paris, June 14–19, to celebrate the centenary of the first production of industrial aluminum in France by Henry Sainte-Claire Deville. The program of the congress will include an official meeting at the Sorbonne in memory of Sainte-Claire Deville; a debate on papers dealing with aluminum metallurgy, the chemistry and physicochemistry of aluminum compounds, and the technology and uses of aluminum and aluminum alloys; and visits to plants and laboratories in Paris and vicinity. The exhibition will consist of displays of aluminum and aluminum products prepared by L'Aluminium Français. Final programs and other relevant information may be obtained by writing the secretary, R. Gadeau, L'Aluminium Français, 34 rue Balzac, Paris 8, France.

The **Electrochemical Society** will hold its 105th meeting at the LaSalle Hotel in Chicago, May 2–6. There will be sessions on: electric insulation; electronics—instrumentation, luminescence, phosphor screen application, rare metals, and semiconductors; electrothermics; industrial electrolytics; and theoretical electrochemistry. There will be 145 papers presented. The program booklet, which includes abstracts, will be available Apr. 1 from the secretary of the Society, Henry B. Linford, 216 W. 102 St., New York 25.

The **Xth International Congress of Agricultural and Food Industries** will be held in Madrid, Spain, from May 30 to June 6. All correspondence should be addressed to the General Secretaryship of the Congress, Zurbano 3, Madrid.

The **19th International Neurologic Reunion,** organized by the French Neurological Society, will be held in Paris, June 1–2. On June 3 the French Neurological Society will hold its usual monthly meeting. The neurologic sequelae of treated tuberculous meningitis is the central problem to be discussed at the International Reunion. Members and associate members of the French Neurological Society are invited to attend and participate in the program. All neurologists who are not members of the French Society but wish to participate in the program of the Reunion should apply *before May 1* to the Secretary-General, Dr. Jean Sigwald, 68, boulevard de Courcelles, Paris (XVII^e).

The 63rd annual meeting of the **Ohio Academy of Science** will be held on the campus of Ohio University as a part of the university's sesquicentennial program, Apr. 15–17. Eleven sectional programs will be presented on Apr. 16 and 17; and the annual Science Day of the Junior Academy will be held on Apr. 16. R. A. Hefner of the Department of Zoology, Miami University, will deliver the presidential address under the title "Selective factors in human survival." Other principal officers of the Academy are: sec., Rush Elliott of Ohio University; treas., R. M. Geist of Capital University.

The **Symposium on Molecular Structure and Spectroscopy,** sponsored jointly by the Graduate School and the Department of Physics and Astronomy of The Ohio State University, will be held June 14–18. This year the Division of Chemical Physics of the American Physical Society will act as cosponsors of the first three days of the symposium. A program of the meeting, which will include abstracts, will be published through the cooperation of the Office of Naval Research. Contributors must submit abstracts *not later than Apr. 29.* For further information write Harald H. Nielsen, Dept. of Physics and Astronomy, The Ohio State University, Columbus, Ohio.

Technical Papers

Movement of Alpha-Methoxyphenylacetic Acid from One Plant to Another Through Their Root Systems

W. H. Preston, Jr., John W. Mitchell, and Wilkins Reeve

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Alpha-methoxyphenylacetic acid (*1*) (MOPA) was recently reported to have marked plant growth-modifying properties and to be readily translocated by bean and some other plants (*2*). In experiments reported here, MOPA (or a derivative of it) moved out of the roots of plants to which it was applied into nearby roots of untreated plants which then translocated it upward and developed modified leaves.

This movement of MOPA from one plant to another was not due to evaporation and movement of the compound through the air such as occur with volatile forms of 2,4-D (*3, 4*). Evaporation from three 1-g portions of MOPA stored at about 70 to 95°F for 4 mo averaged 16 μg/day, which was not sufficient to induce growth effects in young bean plants enclosed for 4 days in airtight bags (3-liter capacity) each with a 1-g portion of MOPA.

In another test, the stem of one plant was treated with 100 μg of MOPA mixed with 1 part of Tween 20 and 4 parts of lanolin applied as a narrow band around the stem. The untreated stem of another plant with roots in a separate pot was fastened 0.5 in. from the treated one by means of a piece of notched cardboard. For comparison, another treated and an untreated plant with their roots in the same pot were also fastened with their stems 0.5 in. apart. Both treated and untreated plants in the same pot showed effects of MOPA within 2 days. Untreated plants with their roots in pots separate from those of treated plants did not show effects of the chemical even after 3 wk.

Detectable amounts of MOPA moved from one plant to another within 9 hr after the chemical was applied. To determine the time required for transfer, 10 groups of 10 young bean plants (two plants in each pot) were selected. To the upper ¼ in. of the hypocotyl of one plant in each pot, 600 μg of MOPA, in the paste carrier previously described, was applied. Treated plants were severed at the soil surface from successive groups at 3-hr intervals after treatment. Subsequent observations showed that untreated plants grown for 9 hr or more in pots with intact treated ones developed malformed leaves, thus indicating transfer of a sufficient amount of MOPA to induce growth modification. The amount of MOPA transferred under the conditions described was equivalent to about 2 to 3 percent of that applied.

To indicate whether MOPA remained unchanged (aside from salt formation) when translocated upward through stems, about 2000 secondary galls induced by direct application of MOPA to stems of snap bean plants were collected (*2*). These were frozen, pulverized, boiled with 5 liters of water, and filtered. The filtrate was concentrated, acidified, and extracted repeatedly with ether, and the ether was evaporated. The resulting mixture of acids (about 1 g) was neutralized with 10 percent sodium hydroxide solution, 1 g of sodium chloride was added, and the *p*H of the solution was adjusted to 3.1. After standing for a few days at 0°C, the sodium acid salt of MOPA, together with small amounts of other acids, was separated. Washing with isopropyl alcohol removed alcohol-soluble impurities and left 25 mg of the sodium acid salt, with sodium chloride as an impurity. The material was treated with hydrochloric acid and extracted with chloroform; evaporation gave 11 mg of crude MOPA. The compound was identified by comparing its melting point (65°C) and mixed melting point (69°C) with that of an authentic sample (71°C), and by means of a methoxyl analysis (*5*) (theory, 18.7 percent; found, 14.8 percent, corresponding to a material 80-percent pure). The amount of MOPA recovered corresponded to 4.5 μg in the secondary gall of each plant. About 200 μg of the crude MOPA thus obtained was applied individually to the stems of young plants. Within 2 days, untreated bean plants in the same pots developed typical MOPA symptoms.

When plants treated with MOPA were grown with their roots in aerated water, the chemical was translocated to the roots and moved out into the water. In demonstrating this, three young bean plants approximately 5 in. tall were supported so that their roots were immersed in about 200 ml of tap water that was aerated by passing compressed air through it. About 400 μg of MOPA was applied to the hypocotyl and first internode of each plant. Three comparable untreated plants were similarly maintained in another container. As the experiment progressed, additional water was added to equal the amount lost from evaporation.

After 1 wk, the plants were removed. The water in which the treated plants had grown was evaporated; the residue was collected in ether, transferred to a vial, and dried. The residue was dispersed in 0.2 ml of water containing 0.01 percent of Tween 20. Four 0.01-ml aliquots of this mixture were then applied separately to the terminal buds of each of four young bean plants. Comparable plants treated with the residue from water in which untreated plants had grown served as controls. Residue from water in which the roots of MOPA-treated plants had grown induced typical MOPA effects. Plants treated with residue from water in which roots of untreated plants had grown were unaffected.

In a similar experiment, treated and untreated plants were grown separately with their roots in

aerated water. After 1 wk, the plants were removed and new plants were substituted. Four days later the trifoliate leaves of those growing in water that had previously supported growth of treated plants showed typical MOPA effects. Width of the modified leaves was 88 percent and their length 79 percent less than that of leaves of plants grown in water that had previously supported the growth of the untreated plants.

Snap bean, sunflower, cucumber, buckwheat, cotton, and corn seeds were germinated together in composted soil in 6-in. clay pots to determine whether MOPA would move from one kind of plant to another through their roots systems. After the pots had been divided into six groups with equal numbers of plants, MOPA was applied in the carrier as a band around the stems of all plants of one species in the first group. Plants of another species were treated in the second group, and so on, until each species (except corn) had been treated and was growing with untreated plants of the remaining species. Corn plants in one group were treated by applying a band of the paste, about 1 cm wide, across the base of the first true leaf. On the basis of the formative effects induced, MOPA moved from bean plants to sunflower, cucumber, buckwheat, and cotton; from cucumber to bean, sunflower, buckwheat, and cotton; from sunflower to bean; from buckwheat to bean; and from cotton to bean. There was no evidence that MOPA moved from corn to any other plants.

A wide variety of growth-modifying compounds known to induce formative effects when applied to bean plants were tested to determine whether they moved from one plant to another through the root systems. In these tests, about 150 to 200 μg of each compound tested was applied in the Tween-20-lanolin carrier as a band around the stem of one of two bean plants growing in the same pot. The following compounds (*6*) were tested: 2-naphthoxyacetic acid; 3,4-xylyloxyacetic acid; 2,4-dibromophenoxyacetic acid, 2,3-dichloropropyl ester; para-chlorophenoxyacetic acid, 2-butenyl ester; para-chlorophenoxyacetic acid, 2-methylallyl ester; 2,4-dichlorophenoxyacetamide; 2,3,5-triiodobenzoic acid; and 2,4-dichlorophenoxyacetic acid and 6 of its salts and esters. In addition, 14 other chlorine-substituted phenoxyacetic acids (*7*) were tested, all of which were known to induce growth modifications when applied directly to bean plants. None of the compounds was moved from the treated plants to the untreated ones in sufficient amounts to induce visible growth effects.

MOPA apparently did not accumulate and remain in detectable amounts in soil in which treated plants were grown. Bean plants treated with about 150 μg of MOPA on the first internodes were removed from soil in which they had grown for 2 wk. Bean seeds were immediately planted in the soil, but the resulting plants did not develop growth modifications.

When a treated and an untreated plant were grown in soil contained in a pot, MOPA may have moved from roots of the treated one through the water films into roots of the untreated one and apparently through those roots that were in contact with each other, or at least through those that grew very near to each other. Close proximity of bean roots was repeatedly observed, sometimes as many as five roots growing in contact with each other for a distance of 1 in. or more.

References and Notes

1. Available from the Polynitro Chemical Co., Box 374, College Park, Md.
2. J. W. Mitchell and W. H. Preston, Jr. *Science* **118**, 518 (1953).
3. P. C. Marth and J. W. Mitchell. *Botan. Gaz.* **110**, 632 (1949).
4. W. R. Mullison and R. W. Hummer. *Botan. Gaz.* **111**, 77 (1949).
5. Carried out by Kathryn Gerdman.
6. Supplied by Chemical-Biological Coordination Center.
7. Supplied by American Chemical Paint Co., Ambler, Pa.

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Central Nervous System Gliogenesis in Piromen-Treated Rat Embryos

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In addition to its pyrogenic properties, the bacterial polysaccharide Piromen has been shown by Windle, *et al.* (*1*) to possess the ability to inhibit glial proliferation in traumatic lesions of the spinal cord and brain of mammals. These investigators employed a dose of 0.5 micrograms per kilogram (μg/kg) of body weight, administered intravenously daily for 2 wk.

Because of these results, we have attempted to inhibit the normal maturation of central nervous system glial tissue in the rat embryo and in the developing rat with Piromen. Since intravenous administration was impractical, relatively large doses were given subcutaneously and intraperitoneally. Fischer females were bred with Agouti males (both are Curtis-Dunning lines). The Piromen treatment schedule was varied in three ways.

A-1. Injections were begun on the 10th to 12th days of pregnancy via the intracardiac or intraperitoneal route. Four animals were treated for 1 to 5 days and received total doses of 4 to 10 μg/kg. Embryos were obtained at the 12th and 15th days of pregnancy and immediately after birth.

A-2. Injections were begun on the 16th to 19th days of pregnancy via the intraperitoneal route. Five animals were treated for 1 to 4 days and received total doses of 0.4 to 1.8 μg/kg. The animals were allowed to come to term, and 25 young rats were sacrificed at postpartum days, 0, 1, 2, 3, 7, 12, and 40.

B. Siblings from animals treated under schedule A-2 were given daily injections after birth. The injections were first made subcutaneously and later intraperitoneally as the animals grew. Three animals sacrificed at the age of 2 or 3 days had received total doses of 0.5 to 2 μg/kg. Nine other animals received

progressively increasing doses during the first 23 days of life, the total dose was 150 to 275 μg/kg. The animals were sacrificed at the age of 39 days.

C. The mothers were not treated. The animals were treated as under schedule B, the total dose was 2.5 to 15 μg/kg in 23 days. There were eight animals in this group. They were sacrificed at 23 or 28 days of age.

Approximately an equal number of embryos and young rats from mothers that received no treatment were sacrificed for control studies. Also, litter mates of young rats receiving Piromen in both groups B and C were given injections of 0.9 percent sodium chloride as a further control measure.

Sections from representative levels of the brain and spinal cord of both the injected and control material were stained by the hematoxylin and eosin, Nissl, phosphotungstic-acid hematoxylin, Cajal gold sublimate, and Hortega silver carbonate methods. A comparison between the injected and the control animals showed no differences in the condition of either glial or neuronal tissues.

Even though large doses of Piromen were given at a time when gliogenesis was taking place, we could discern no effect from its administration in the manner described. We are unable to answer the possible questions whether Piromen crosses the placental barrier and reaches the central nervous system of the embryos, or whether an adequate concentration of Piromen is produced in the central nervous system by intraperitoneal or subcutaneous administration.

Reference

1. W. F. Windle, C. D. Clemente, D. Scott, Jr., and W. W. Chambers. *Induction of neuronal regeneration in the central nervous system of animals* (Tr. Amer. Neur. Assoc., 1952), pp. 164–170.

Received December 7, 1953.

Development of Lymphoid Tumors in Nonirradiated Thymic Grafts in Thymectomized Irradiated Mice[1]

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Lymphoid tumors and lymphatic leukemias arising either spontaneously or in response to exogenous agents (x-rays, estrogens) tend to originate in the thymus in several mouse strains (*1–3*), and their incidence may be drastically reduced by thymectomy (*1–6*). That the effect of thymectomy is not due simply to removal of potentially malignant cells was demonstrated by Law and Miller (*7*), who found that lymphatic leukemia incidence in methylcholanthrene-treated dba mice could be restored to control levels by autologous or homologus thymic implants, although the implants were seldom involved by the leukemic process. This observation was recently confirmed when Kaplan, *et al.* (*8*) noted a significant increase in lymphoid tumor incidence in thymectomized, irradiated C 57 black mice bearing homologous thymic implants.

FIG. 1. Arrow points to lymphoid tumor mass replacing thymic implant. All other lymphoid tissues were microscopically normal. (×3)

An experiment was then set up to test the influence of such factors as the age of the thymic implants and the time of their implantation on tumor response. The complete experimental design is not pertinent to the present report, which is concerned only with those groups that were treated essentially as follows: C 57 black mice, segregated by sex, were thymectomized by our usual technique (*5*) at 30 to 40 days of age and were started on whole-body irradiation 2 to 7 days later. They received four doses of 168 r each at 8-day intervals; physical factors were: 120 kv, 9 ma, 0.25 mm Cu + 1.0 mm Al added filter, 30 cm mouse-target distance, 32 r/min. Thymus glands were rapidly excised from intact, nonirradiated 33-day-old C 57 black donors and were immediately implanted subcutaneously in the right axillary region of each recipient mouse. Most grafts were made within 1 hr after the last irradiation, but mice of two groups received implants 1 and 8 days, respectively, after irradiation.

Tumors were observed as early as 4 mo after thymic implantation, but most of these had disseminated by

[1] This investigation was supported by grants-in-aid from the National Cancer Institute, National Institutes of Health, U.S. Public Health Service, and the Jane Coffin Childs Memorial Fund for Medical Research.

the time they were detected, and it was not possible to determine their site of origin. More recently, however, a small firm nodular mass was palpated at the site of thymic implantation in three animals (two male, one female) in whom grafts had been made promptly after irradiation, about 5 mo earlier. These mice were immediately sacrificed and carefully autopsied. Each bore a nodular opalescent whitish mass in the subcutaneous tissues of the right chest wall, below the axilla, which had the gross appearance of a lymphoma. Neither the immediately adjacent right axillary lymph nodes nor the more remote superficial nodes were enlarged. On opening the thorax, there was no visible residue of the autologous (excised) thymus. The mediastinal nodes were not enlarged, and the lungs appeared normal. There was no microscopic abnormality of the abdominal viscera, except for the usual post-radiation atrophy of the ovaries and uterus of the female mouse.

The tumor masses, superficial, mediastinal, and mesenteric lymph nodes, spleen, lungs, one kidney and adrenal, and a portion of the liver were fixed in Bouin's fluid, sectioned, and stained with hematoxylin and eosin. Microscopic study revealed typical lymphosarcomas, identical with those previously described (*9*), replacing one or both lobes of the thymic implants, with invasion beyond the capsule and into the intercostal muscles in one instance. There was no evidence whatever of tumor infiltration in any of the other tissues. To date, tumors grossly confined to the implant have been observed in more than a dozen animals of which four received a thymic graft 1 day, and one as late as 8 days, after irradiation (Fig. 1).

It seems clear that the site of origin of these lymphoid tumors was in the thymic implants, which received no radiation at any time. To the best of our knowledge, this represents the first definitive instance of the induction of a malignant tumor in a tissue that has not been exposed to the carcinogenic agent responsible for the neoplastic change. The observation establishes the existence of a completely indirect mechanism of induction of lymphoid tumors in systemically irradiated mice, in which the role played by the thymus appears to be a dual one. In some strains, although not in all, the thymus is the site of origin of the malignant lymphoid cells, and in all strains thus far studied, it appears to contribute an influence necessary for the development of lymphomas and lymphatic leukemias, even when it is not involved by the tumor process (*7*).

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Hemagglutination by *Clostridium botulinum* Type D

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Lamanna (*1*) showed that hemagglutination of red cells by supernatants of *Clostridium botulinum* type C cultures was specific in the sense that the reaction could be inhibited by antiserum to type C, but not by antisera to types A and B. This result is additional evidence of the considerable differences existing between these types, as exemplified by their cultural, biochemical, and toxigenic dissimilarities. However, the greater similarity of types C and D suggested that a common hemagglutinating factor might occur, and, accordingly, a number of experiments were carried out to test this possibility.

Table 1 summarizes the results of a typical experiment with a type-D "toxin."

TABLE 1. Typical experiment with a type-D "toxin."

Antiserum used	Results (end-point of dilution of serum showing inhibition of hemagglutination)
Cl. botulinum type D	Complete inhibition to dilution of 1/384
Cl. botulinum type C	Complete inhibition to dilution of 1/768
Cl. perfringens	Partial inhibition to dilution of 1/12
Cl. edematiens	Partial inhibition to dilution of 1/12
Cl. septicum	No inhibition
6 Normal Sera	No inhibition

The *Cl. botulinum* type-C and type-D antisera used in the tests on hemagglutination inhibition were from hyperimmunized horses and had high antitoxic titers. Although it is not unusual for high-titer type-C antisera to contain a small amount of antibody to type-D toxin, and vice versa, this particular type-C antiserum contained no detectable antibody to type-D toxin. The type-D toxin was a solution of a dry, partially purified filtrate of a *Cl. botulinum* type-D culture and was employed in the test at twice the concentration that gave complete agglutination of sheep cells in the system used.

Clearly, hemagglutination of sheep cells by the type-D filtrate was inhibited by antisera to both types D and C. It is noteworthy that type C (the heterologous) antiserum was the more potent in this respect—a finding that was constant in all the experiments with these antisera. This particular type-C antiserum contained no demonstrable antibody to the toxin of type D.

It is also of interest that high concentrations of a *Cl. perfringens* and a *Cl. edematiens* antiserum gave a partial inhibition of hemagglutination, although the

donors of these sera had never, so far as was known, been exposed to botulinum antigens and possessed no demonstrable botulinum antitoxins.

The results summarized here are additional evidence of the closer relationship existing between *Cl. botulinum* types C and D than that between types A, B, and C. And they emphasize, in addition, that the lethal toxin and hemagglutinin are not the same.

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Nuclear Emulsions for Electron Microscopy[1]

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The identification of radioactive mineral grains using "Nuclear Research" emulsions and a petrographic microscope is limited to those grains within the resolving power of the microscope. Frequently there is need for the higher resolving power of the electron microscope to make accurate size measurements and study the morphology of these grains.

A technic has been devised to obtain emulsions thin enough to allow transmission of the electron beam, yet containing a sufficiently heavy and uniform concentration of silver bromide crystals to permit the recording of alpha-particle tracks. The technic makes use of Ilford C2 emulsions in gel form. A small quantity of the gel is heated to 50° C in a glass beaker, according to the directions of the manufacturer. When the gel is fluid, approximately 0.025 ml is removed from the beaker with a blood pipet and deposited on a 1 × 3 in. Formvar-coated glass slide. The finely ground sample, the amount used being determined by trial, is mixed with the gel which is then spread uniformly over the surface of the slide by means of a curved stainless steel spatula.[2] An alternative method of adding the sample is to sprinkle the mineral grains over the moist surface of the gel after the slide has been coated. This latter method reduces the possibility of forming silver tracks by pressure of the mineral grains in the silver bromide crystals as the gel is spread over the surface of the glass slide. The volume of gel placed on the slide takes into account loss due to adhesion to the spatula. It is extremely important that the entire procedure, from the removal of the measured amount of gel to the formation of the film on the slide, be carried out rapidly before the gel starts to set or fogging due to pressure of the spatula will result. This time period was found to be less than 1 min. With practice, it is a relatively simple matter to obtain emulsions of consistent thickness. After the emulsion has been prepared it is stored in a light-tight cabinet for a predetermined length of time. For highly active uraninite, an exposure of from 3 to 4 days yielded numerous alpha tracks. The exposed emulsions are developed for 2 min in Eastman Kodak D-8 developer, fixed for 15 min in a standard fixer, and then washed and dried. They are then scored with a sharp blade to divide them into ½-in. squares. The squares of emulsion are floated from the glass slide by placing the slide in a Formvar solvent, ethylene dichloride. After washing in fresh solvent, they are picked up on sections of stainless steel screen and are carefully placed in steam for 1 to 2 min to obtain better adhesion of the gelatin to the screen. At this point suitable areas for the electron microscope may be chosen by examination in an optical microscope and marked. Disks ⅛ in. in diameter are cut from the marked areas by means of a punch. The thickness of an average emulsion prepared in this manner was measured by shadow-casting sections on collodion substrates and was found to be approximately 0.2 μ.

If it is desired to attempt identification of the mineral grains in the emulsions by selected area diffraction in the RCA or Philips electron microscope, it is advisable to remove the gelatin. This can be done in an enzyme if the emulsion is fixed in a 30-percent solution of sodium thiosulphate containing no hardener. Sections of the developed emulsion are picked up on collodion substrates supported on the stainless steel screens. These are carefully immersed in a freshly-prepared 0.5 percent solution of Taka-Diastase at room temperature for 10 min. Some emulsions may require a more concentrated solution. They are then washed

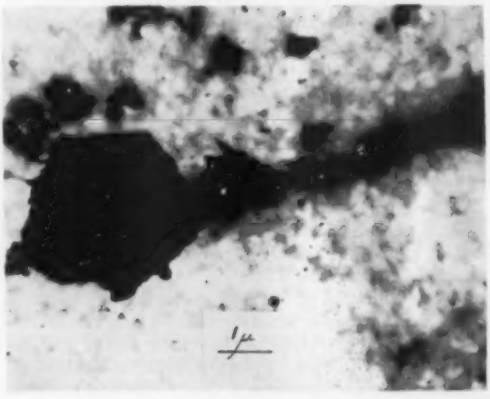

FIG. 1. Electron micrograph of a Carnotite particle with an alpha track. The small opaque particles scattered throughout the field are silver grains caused by normal fogging of the emulsion and are not associated with radioactive particles. The diameter of the Carnotite particle is approximately 3 μ.

[1] This work has been supported by the Division of Research of the U.S. Atomic Energy Commission and is part of a research project directed by Dr. T. F. Bates and concerned with the study of uranium in the Chattanooga shale. Contribution No. 53-50 from the College of Mineral Industries, The Pennsylvania State University, State College, Pa.

[2] Sold under the trade name, Scoopula, by Fisher Scientific Co., Pittsburgh, Pa.

in two to three changes of distilled water and dried, care being taken not to move the screens any more than is necessary. If the proper care is exercised, the gelatin is completely removed by the enzyme, thus leaving on the substrate the mineral grains and any tracks emanating from them which may have been there before removal of the gelatin. Success in obtaining single crystal patterns will be limited to those particles thin enough for transmission by the electron beam. Ring patterns should be of value if fields can be obtained in which there are high enough ratios of active grains to inactive ones to make identification possible.

Electron micrographs (Figs. 1 and 2) indicate that

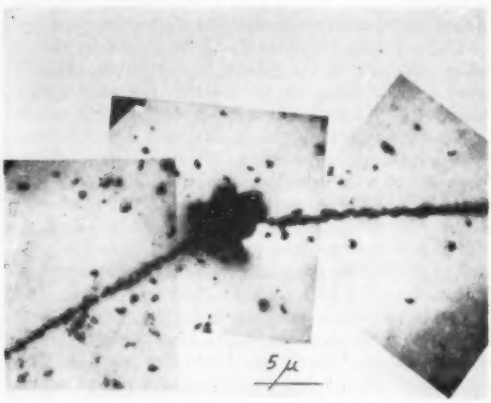

FIG. 2. Electron micrograph of an Uraninite fragment with associated alpha tracks. The mottled background is characteristic of these emulsions and is believed due to variations in the thickness of the gelatin film caused by the silver bromide particles originally embedded within it. The diameter of the Uraninite fragment is approximately 5 μ.

the emulsion contains a sufficient concentration of silver bromide crystals to yield continuous tracks. It is seen that there is some lack of sharpness around the edges of the mineral grains because of the surrounding film of gelatin. This occurs even when the grains are dispersed on top of the soft gelatin rather than within it.

The present technic allows one to study the size and shape of radioactive minerals identified by their alpha tracks. It does not, however, permit one to distinguish nonradioactive grains from the radioactive ones because the thinness of the film prevents the recording of all alpha particles emitted from a given grain. The maximum angle an alpha particle from a grain resting on the Formvar base may make with the surface of the emulsion and produce a discernible track, about 2 μ in length, may be as low as 5 to 6°. If it is assumed that most of the mineral grains are at a depth of 0.1 μ in the emulsion, this angle is reduced to about 3°. Because of this consequent reduction in the number of alpha tracks recorded for a given grain, it is not feasible to regard the usual lower limit of at least two radial tracks from a single grain as the criterion for judging a grain to be radioactive.[3]

[3] Yagoda, H. *Radioactive Measurements with Nuclear Emulsions.* p. 177. New York: Wiley, 1949.

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Temperature Dependence of Rattling Frequency in the Rattlesnake, *Crotalus v. viridis*

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It has been generally appreciated that the rate of rattling of a poikilotherm snake is likely to depend upon the temperature of the animal. However, although isolated records of this rate at a particular temperature can be found in the literature, exact comparisons over a large temperature range are missing except for the report of Klauber (*1*), who observed in *Crotalus v. viridis* an average increase of 93 cpm/° C between external temperatures of 11 and 22° C. In Klauber's measurements, the motion was recorded on a smoked drum by means of a pin attached to the rattle.

In the fall of 1941 we had an opportunity to study 18 adult male and female *C. v. viridis* recently removed from a hibernating den located near Cheyenne, Wyoming. These were collected and sent through the kindness of Dr. George L. Baxter of the University of Wyoming.

Rattling frequency was determined with the aid of a mercury arc stroboscope light. The snakes were placed in an icebox at 5° C or in an incubator at 37° C and left there 1–2 hr. Immediately after these exposures, a thermometer was inserted at least 6 cm into the cloaca. Temperature and frequency readings were then made simultaneously while the animal slowly warmed or cooled.

The grouped results of 226 observations at various body temperatures are shown in Fig. 1. The line fitted to the averages by the method of least squares describes an empirical relationship where the rattle frequency in cpm is equal to $155T - 283$, T being the temperature in degrees centigrade.

Of interest is the linear nature of the relationship over the large temperature range, as well as the high frequencies with which a poikilotherm vertebrate is able to respond not only at temperatures approaching those of warm-blooded animals but also at normal environmental temperatures. By extrapolating the curve 5°, a frequency of 100 cps at 41° C is obtained. This may be compared with the frequency of the humming bird wing beat of about 75 cps at a similar body temperature, or with the wing-beat frequencies of various insects (*2*).

[1] Present address: Medical Laboratories, Army Chemical Center, Maryland.

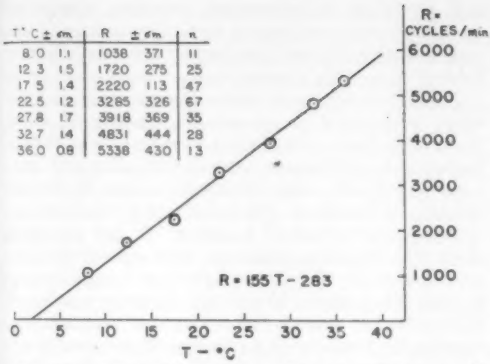

FIG. 1. Relationship between body temperature and rattling frequency in *Crotalus*.

The to and fro movement of the rattle is accomplished by 3 large muscle groups on each side Their fibers run diagonally, the origin and insertion connecting successive tail vertebrae. All 3 muscle groups on each side contract simultaneously during rattling. This has been determined by recording the action potentials of the several muscle groups simultaneously. The potentials were led off insulated needle electrodes that were inserted into the muscle tissue and isolated by an indifferent ring electrode. Frequencies of these electrical recordings were the same as those of the actual rattle movements observed simultaneously under the stroboscope. These observations, which were made in collaboration with Dr. E. B. Wright, suggest that there is no sequential alternation of contractions in the 3 muscle groups which might account for the high frequencies of rattling observed.

It is also of interest to point out that these tail muscles are dark red to brown in color, in distinct contrast to the other skeletal muscles of the body, which are white to light pink. This suggests the possibility of a high content of muscle hemoglobin or other respiratory pigment (*3*) which might be essential not only for the high frequencies but also for the long duration of uninterrupted rattling that is sometimes observed. Continuous rattling for periods as long as 20 min has been reported (*1*).

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A Technic for Shipping Live Mosquitoes with Particular Reference to *Culex tarsalis*

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Experience in isolation of viruses from mosquitoes has demonstrated the desirability of fresh material for test purposes. Even with the resistant western equine encephalitis virus a drop in titer may occur during prolonged storage of infected *Culex tarsalis* in dry-ice chests. In connection with virus encephalitis investigations at the Rocky Mountain Laboratory, our attention was centered on an adequate and practical method of transporting living female mosquitoes from considerable distances afield to the virus laboratory.

The first attempt to transfer mosquitoes over a long distance to our laboratory was made in the summer of 1952 when specimens freshly collected in Glasgow, Montana, were conveyed by automobile to Hamilton, Montana, a distance of some 500 mi. The mosquitoes, in the bags in which they were collected, were carried in a portable icebox, but out of direct contact with the ice. The elapsed time from packing to unpacking was about 28 hr. Mortality was negligible, and the mosquitoes were as active as when collected. The next attempt was made by shipping *C. tarsalis* females by Railway Express from Bismarck, North Dakota, to Hamilton, Montana, some 800 mi. The bags of mosquitoes were packed in a small carton within a large carton. Refrigeration was provided by Mason jars of water frozen solid by CO_2. Sawdust and newspapers furnished the necessary insulation. The elapsed time from packing to unpacking was about 39 hr. Again, mortality was negligible and the mosquitoes were active and vigorous on arrival.

Encouraged by the results of these trials, we have developed the shipping technic described below.

The dual-purpose collecting and shipping bag is a type widely used and is simply a cylindrical muslin bag with a window of bobbinet forming the closed end. The dimensions of the bag are accommodated to a supporting inner wire frame that forms the outlines of a right cylinder. This frame, of 3/32-in. Monel wire, consists of two 4½-in. rings, with parallel planes and on the same axis, held in position by a single vertical wire 8½ in. long. The bag is closed by rubber bands. For shipping purposes a bag of this size will hold up to 300 mosquitoes without crowding. It is desirable that a schedule be arranged whereby mosquitoes may be collected shortly before packing and shipping.

One or two bags of mosquitoes are placed in a substantial paper carton of a size that will permit the inclusion of a refrigerating medium. We have found Sno-Gel Refreezants,[3] model R10-B, to be an adequate

[1] National Institutes of Health, National Microbiological Institute, Rocky Mountain Laboratory, Hamilton, Montana.
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[3] Manufactured by Sno-Gel, Inc., 334 Magnolia St., Oakland 20, Calif. "Refreezants are a harmless, odorless substance holding liquid in colloidal suspension." Model R10-B is such a substance in a cylindrical plastic skin about 10 by 2 in., sausage-like in appearance, freezing at 30° F. These can be frozen either in deep-freeze units or more quickly with dry ice, and can be reused indefinitely.

substitute for ice, and superior to ice in many respects because of less weight and volume, durability, and no free moisture. Two units are placed in the carton separated from the mosquitoes by a pasteboard partition. Any remaining space is packed with insulating material. This carton is sealed and centered in additional insulating material within a much larger carton (a standard 24-bottle beer case is a satisfactory size and is well made). We use mineral wool insulating blankets, of the type commonly used in building construction, sometimes supplemented by wadded newspaper. The outer carton, when sealed and wrapped in heavy brown paper, is ready for shipment.

In laboratory tests and in actual practice we have observed that in summer or at room temperature the effectiveness of the refrigerant, under the conditions described above, decreases gradually up to 50 hr and by 72 hr is lost. At this point a sudden rise in mosquito mortality may be expected, and usually occurs, so that the survival rate at 3 days is 80 percent or less. At 4 and 5 days mortality was excessive, in some cases 100 percent; invariably it was over 50 percent. Increasing the number of Refreezant units to 3 and to 4, and providing supplementary humidity, either by dampening mosquito bags or by adding moistened absorbent cotton, did not significantly alter the effective holding time or the survival rate.

Twenty-two shipments of live mosquitoes have been made, principally by air express. Twenty of these were to the Rocky Mountain Laboratory from Washington, eastern Montana, western Nebraska, and Arizona, and 2 were colony mosquitoes from Hamilton, Montana to Maryland. The number of mosquitoes per shipment varied from 30 to nearly 700 and averaged about 300. Nineteen shipments were considered successful. Mortality for the most part was negligible and in none did it exceed 15 percent. In the remaining 3 shipments, for reasons that we cannot satisfactorily explain, the mortality rate exceeded 50 percent. In all shipments the elapsed time from packing to unpacking was less than 60 hr and in most cases less than 36 hr.

In spite of the limitation imposed by the time factor of 3 days or less, we have found this shipping technic to be very useful, and feel that we are not premature in recommending it to others.

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Communications

Group Research

In an article on "Free Research versus Design Research" [*Science* **118**, 91 (1953)], Curt P. Richter examined the present policy governing allocation of grants-in-aid to research workers and, *inter alia*, used the occasion to deplore the present trend toward team or group research, which was represented by him as out of harmony with scientific tradition and as a somewhat naive tactic introduced by those who themselves understand little of the ways of scientists. Since group research involves an arrangement by which at least two persons undertake to solve a problem in concert, it is obvious that there will be almost as many arrangements as there are persons and that, before a fair evaluation of group research is possible, some effort has to be made to recognize the different ways in which such research has been and is carried out.

By and large, the theoretical scientist in all fields is a "rugged individualist" and has always been so. Collaboration between two theorists in the same field would be like collaboration between two champion chess players. They would hardly complement each other and, very likely, would just get in each other's hair. The very opposite tradition has always prevailed in the experimental sciences. Some of the greatest experimentalists of all times—Pasteur, Lavoisier, Rutherford, J. J. Thomson, T. H. Morgan, Emil Fischer, O. Meyerhof—thoroughly enjoyed working intimately with a band of colleagues and, in many cases, owed much of their success as experimentalists to the qualities that some of their colleagues possessed.

Why has group research found favor among the experimentalists? It is, I believe, the consequence of the fact that the major problems of the experimental sciences are usually far beyond the capacity of any one individual, however gifted, to solve unaided even after a lifetime of work. Consider a relatively straightforward problem, such as the mode of action of insulin. Despite heroic efforts by many workers in laboratories all over the world, this problem had still eluded solution. A vast number of hypotheses have been advanced, but a prodigious effort is involved in testing each one. Some hypotheses cannot even be tested with present methods and must await further technical advances. Major problems of experimental science are like giant jigsaw puzzles, which cannot be solved until hundreds of individual pieces are placed together in the proper patterns, and the placing together of any two pieces is a problem of no mean proportions. Clearly, when the over-all problem has so many facets, the chances of solution are roughly proportional to the number of facets investigated. The single investigator just cannot cope with the volume of experimentation, of trial-and-error search needed to find the necessary clues. Thus, it is not a question of whether group research is necessary in experimental science, but rather of what kind of group research works best.

Group research has come to mean to some a grotesque arrangement whereby some dictator in his office directs the energies of an army of research stooges in the laboratory by push-button control. If this is what group research is taken to be, then nobody in his right mind can make out a case for such a monstrosity. If, however, group research is looked upon as an effort

by a group of individuals to solve collectively a problem which no one of the individuals could expect to solve singlehandedly, then group research falls in line with a long tradition in experimental science.

Group research is not only a scientific venture but also an experiment in human relationships. In the ideal group, such as existed in the laboratories of some great experimentalists, petty jealousies were minimized and the creative skills of all members were used to the fullest. The proper leader of a research group should be interested primarily in solving a problem. Anyone who can contribute to this end must be encouraged. A group dedicated to the solution of a problem, governed by the conviction that seniority, title, and rank are irrelevant issues in the evaluation of ideas and suggestions, and convinced that the fortune of the individual is tied up with the fortune of the group as a whole is, I believe, one of the most powerful instruments yet devised for conducting experimental research.

The standards of modern science impose an almost herculean burden on the lone investigator. For example, the successful prosecution of any of a large number of biochemical problems requires considerable competence in the techniques of protein fractionation, organic syntheses, manometry, spectrophotometry, and chromatography and in the fields of analytic, organic, physical, and biological chemistry. There have been and probably will be a few giants who will be equal to such all-but-impossible assignments. However, the great mass of investigators can be effective only by dint of specialization. Thus, group work provides one of the few devices by which the efforts of specialists can be integrated and unified and by which skills, useless when uncomplemented, can be fully utilized.

There is a vague uneasy feeling among some scientists that group research means the end of the individual. All research in the end is individual research, and group research conducted properly refers to individuals working together with other individuals. Any tactic that does violence to the rights, privileges, and sensibilities of the individual should be as abhorrent to the group as to the individual. Group research has often foundered on the rocks because the leader has failed in his duties to the individual members of the group by being arbitrary and inflexible or by suppressing differences of opinion. Where group research has prospered, the rights of the individual have rarely been neglected.

In tackling a major experimental problem, there is no telling from which direction a solution may come. The individual, perforce, is limited to a single choice; and, while he may show superior discrimination in the exercise of this choice, he is at a great disadvantage *vis-a-vis* a group where multiple choices may be made and followed up simultaneously. One can be more daring and enterprising in a group where multiple failures for several individuals can be compensated by at least one successful venture by another in the group. If the individual has to carry alone the weight of failure which can be more equitable distributed within a group, he is not likely to undertake a problem that holds forth prospects of more than a fair share of unrewarded exploratory work and experimental dead ends.

There is ample room in our scientific life for both individual and group research. The nature of the problems, of the individuals, and of the physical setup should be the determining factors in deciding which arrangement should be followed, and not a cut-and-dried formula that science can prosper only by leaving the individual to his own devices.

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Contribution to the Chemistry of Thorium and Morin

THE U.S. Geological Survey has been studying the reaction of thorium with organic compounds in a search for a highly sensitive and, if possible, selective reagent for the quantitative determination of trace amounts of thorium. One phase of this investigation consisted of a spectrophotometric and fluorimetric study of the complex formed in the reaction between thorium and morin. Morin is 2′,3,4′,5,7-pentahydroxyflavone ($C_{15}H_{10}O_7$).

In weakly acid solutions, the stable complex $Th(morin)_2$ with a dissociation constant of approximately 2×10^{-10} is formed. The sensitivity of the reaction is such that 0.1 to 0.2 μg of ThO_2 in 50 ml of solution can be determined either colorimetrically or fluorimetrically. The color system follows Beer's law; and, under proper conditions, the fluorescence shows a linear relationship with the concentration of thorium over a wide range. Morin is about 2½ times as sensitive to thorium as thoron, 1-(O-arsonophenyllazo),-2-naphthol-3,6,-disulfonic acid ($C_{16}H_{13}O_{10}N_2S_2As$), which is the most sensitive reagent generally available. So far, morin has been used only with pure solutions of thorium, but the reaction could be used as the starting point in the development of methods for the quantitative determination of trace amounts of thorium in rocks and other materials.

In the course of this work, the fundamental relationship between the fluorescence and light absorption was studied, and a mathematical equation was derived to express this relationship. Uncombined morin in the solution affects the fluorescence produced in two opposing ways. The amount of complex formed from a given amount of thorium is a direct function of the amount of free morin, whereas the amount of fluorescence obtainable from a given amount of complex is an inverse function of the amount of free morin. The inverse function results from quenching by the morin, and an equation has been derived that relates the amount of fluorescence obtained to the amount of free morin. The relationship is hyperbolic and similar to that shown by other fluorescent systems reported in the literature.

In addition to their theoretical significance, these mathematical functions were directly applicable for determining the proper concentration of morin in the fluorescent system. The combined effects of the opposing functions indicated the one region of free morin content that gives linearity and also maximum sensitivity for this system. Working curves prepared with this optimum amount of morin are linear over a wide range of thorium concentration.

A transmission fluorimeter was designed and built for use in this investigation. Its light source, sample cell, and phototube are arranged on a linear axis with a lamp and phototube on opposite sides of the sample. This arrangement is superior to that of conventional fluorimeters for theoretical studies, because it simplifies the development of the mathematical relationships of light absorption and fluorescence.

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Ground Water in the High Plains of West-Central United States

THE vast High Plains of the west-central United States constitute a region of transition—rather abrupt transition—between the humid East and the arid Southwest. Here, water problems are the more trying because, from year to year, the region "vacillates" between a semiarid or arid environment and a moist subhumid environment. Here, then, "average" water conditions can be misleading indeed.

The High Plains are unique in many respects. Once the grass-covered home of buffalo and nomadic Indians, they were conquered and settled first by cattlemen, who found the virgin grasses ideal for stock raising; then by dry-farmers, encouraged by the Homestead Acts, who discovered the high fertility of the soil; and finally by farmers who found that in parts of the area the uncertainties of meager precipitation could be offset by irrigation—first from streams and later from wells. To a growing agricultural development, discoveries of large oil and gas fields have added substantial industrial development.

The agricultural development has not been without failure and hardship, for nature has tried many times to undo man's accomplishments and often has succeeded over all but the most persevering. Severe drouths and dust storms have ruined dry-farming periodically, but, thanks to irrigation (largely from wells), a stable and prosperous agricultural economy has been established at many places.

Available information indicates that the groundwater reservoir beneath the High Plains probably contains more than 2 billion acre-ft. An estimated 2,700,000 acres now is irrigated by pumping from about 26,000 irrigation wells. The Llano Estacado in Texas and New Mexico, the most heavily pumped part of the High Plains, typifies a large part of the area where ground water is the sole source of supply. Some areas remain undeveloped but some are overdeveloped.

Basic information, collected and studied over a period of more than 20 years by the U.S. Geological Survey, in cooperation with the several States, has materially aided the understanding and orderly development of ground-water resources, but much more investigation and study are needed to realize full development.

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Received March 8, 1954.

Preliminary Report on the Geology of the Aleutian Islands

SINCE 1946 the U.S. Geological Survey, in cooperation with the Department of Defense, has been making a reconnaissance study of the geology of the Aleutian Islands. The Aleutian Islands form a volcanic island arc extending 700 mi westward from the Alaska Peninsula. A deep submarine trough, the Aleutian Trench, lies along the southern convex side of the arc. The northern concave side is marked by a line of stratovolcanoes and is bounded, in part, by a steep scarp that extends to the floor of the Bering Sea.

The oldest rocks crop out on Attu, Agattu, Rat Island, and Amchitka in the western Aleutians and along the southern edge of many of the central and eastern Aleutian Islands. The association of rocks is typical of volcanic geosynclines in orogenic zones and consists of a thick sequence of pillow lava, submarine pyroclastics, siliceous mudstones, argillite, sandstone, and conglomerate. The pillow lavas are basaltic and spilitic. Many of the submarine tuffs are keratophyres. These oldest rocks have yielded no identifiable fossils, and they differ somewhat in lithology from island to island; neither their age nor their interisland correlation is known. On Attu and Amchitka an unconformity separates them from overlying rocks containing early Tertiary fossils.

On Attu and Amchitka, the spilitic suite is overlain by several thousand feet of conglomerate and banded, well-bedded siliceous mudstones, argillite, sandstone, and limestone, all deposited in shallow water. Foraminifera suggest an Eocene-Oligocene age. Rocks of early Tertiary age have not been recognized in the central and eastern Aleutians.

Both the spilitic rocks and the early Tertiary sedimentary rocks of the western Aleutians have been intruded by dikes, sills, and small plutons of gabbro and by a few stocks of albite granite. Batholiths and stocks of diorite and quartz diorite have been found in the central and eastern Aleutians. In general, the intrusive rocks of the Aleutian Islands belong to the calc-alkalic circum-Pacific suite.

Unconformities younger than the plutonic intrusive activity have been mapped on Attu, Kiska, Umnak,

and Adak. These unconformities cut across the spilitic sequence and early Tertiary marine sediments on Attu, the early Tertiary sediments on Kiska, and the old deformed marine sediments and pillow lavas on Umnak and Adak Islands. On Attu, subaerial conglomerate and lava flows overlie the unconformity. On the other islands, lava flows associated with the late Tertiary to Recent stratovolcanoes overlie the unconformities. Unalaska has both deeply eroded dioritic batholiths and a stratovolcano, but an unconformable contact between the two has not yet been found.

Paleontological evidence for confidently correlating the various unconformities is lacking. All of them, however, are overlain by subaerial volcanic rocks and underlain by marine sediments and geosynclinal volcanic rocks. Although these unconformities perhaps differ somewhat in age from island to island, they seem to represent a major uplift of probable middle Tertiary age that extended the length of the Aleutian chain and, perhaps, signaled the birth of the present Aleutian Island Arc.

Normal faults and broad open folds characterize the structure of the Aleutian Islands. Evidences of deep burial or strong compressional tectonic forces, such as thrust faults, isoclinal folds, or strong regional metamorphism, are absent. Most of the faulting occurred during the middle Tertiary uplift, but some faulting has continued to the present.

The late Tertiary to Recent history is one of stratovolcanism involving eruption of calc-alkalic rocks, severe glaciation, and several changes in sea level relative to the land. Today, the Aleutian Island Arc is an area of many active volcanoes and earthquakes, a restless segment of the earth's crust, that contains a record of volcanism and crustal deformation beginning in pre-Tertiary time.

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Long-Term Recovery of Metabolic Products from Rats[1]

FOR many metabolic studies in rats, it is desirable to collect quantitatively, for periods of several weeks, respiratory gases and unmixed excreta uncontaminated with food. A technic has been developed that accomplishes this and avoids any possibility of cross-contamination between urine and feces. Without interrupting collections, blood may be withdrawn and materials may be injected intravenously, intraperitoneally, or subcutaneously.

The hindquarters of an animal are enclosed in a plaster of paris cast, which extends upward to support a bottomless wide-mouthed glass jar of appropriate size that is placed around the animal's head and forequarters (Fig. 1). An airtight seal between the animal and the glass jar is made by cementing a 1-in.-wide belt of sheet rubber around the shaved body of the anesthetized animal midway between the front and hind legs. A sleeve of sheet rubber is cemented to this belt and turned up over the outside bottom of the jar. Enough cotton sheet wadding is wrapped around the body to allow freedom for breathing but, at the same time, to restrict the animal so that it cannot reach and damage the rubber sleeve with its claws or teeth. Better results are obtained if the cast is not padded about the legs. While the cast is being applied over the sheet wadding, jar, and hindquarters of the animal, the hind legs are extended at right angles in the same horizontal plane as the trunk. To prevent contamination of the cast and resulting loss of the excreted products, the plaster is cut away liberally around the external excretory organs.

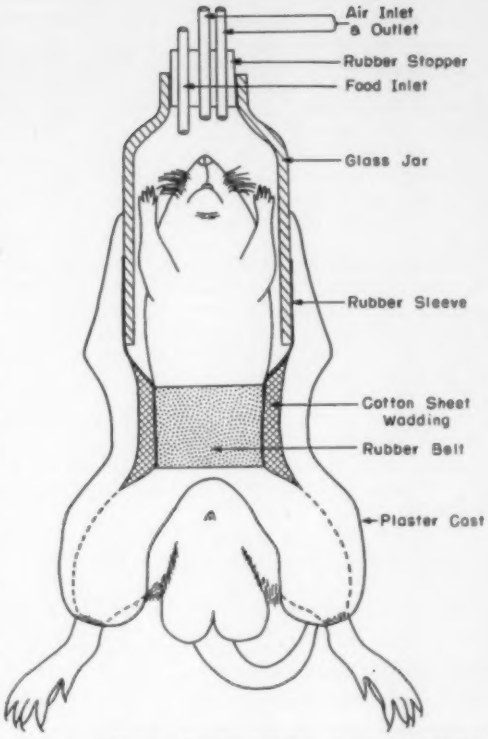

FIG. 1. Diagram showing position of rat with relation to other parts of the assembly.

The encased animal is suspended over small beakers that serve as collecting dishes for the excreta. Complete separation and collection of urine and feces are easily accomplished with male animals but may be less successful with females. The mouth of the glass jar is closed with a rubber stopper that has three holes,

[1] This research has been aided by grants from the Otho S. A. Sprague Memorial Institute and the Douglas Smith Foundation for Medical Research of the University of Chicago.

one of which is used for the introduction of food, and the other two for the inlet and outlet of air.

Food is prepared as a paste and forced into the jar with a syringe. A healthy animal keeps itself and the sides of the jar clean. Food cannot collect under the animal if the front of the jar is tilted slightly downward. The outlet hole is connected to the appropriate collecting system, which is maintained under sufficient negative pressure, from a vacuum line, to provide an adequate supply of air to the animal.

Animals have been maintained without ill effects in this assembly for as long as 3 wk. It appears that the time could be extended indefinitely. The disadvantage of such a system is the enforced inactivity of the animal, which brings about changes in energy requirements and may alter the metabolic pattern of a material under investigation (*1*).

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Reference

1. DEITRICK, J. E., G. D. WHEDON, and E. SHORR. *Am. J. Med.* **4**, 3 (1948).

Received January 28, 1954.

The Smaller Foraminifera in Correlation and Paleoecology

PROBLEMS arising in connection with the study of assemblages of western and central Pacific smaller Foraminifera of Cenozoic age have brought into focus certain advantages and disadvantages of these organisms in age determination, stratigraphic correlation, and paleoecologic interpretation.

Benthonic (bottom-dwelling) species, so far as is known, are characteristically responsive to variation in the sedimentary environment even between closely juxtaposed depositional sites. At the same time, they may be little affected by age difference, even as great as that between Miocene and Recent epochs.

Planktonic (floating) species are subject to wide and geologically rapid dispersal by ocean currents and, thus, should be well suited for use in long-range correlation. The planktonic species, however, are generally limited in their occurrence to open-sea facies and, thus, are available for correlation only between such facies. Planktonic species are commonly good indicators of temperature and may be interpreted to suggest direction of flow of oceanic currents, but they have little bearing on bottom paleoecology except as contributors to the sediment.

Benthonic species, on the other hand, are commonly provincial and may become good local paleoecologic indicators with further knowledge of their living habits and associations.

The apparent correlation of seemingly identical but widely separated planktonic assemblages is commonly weakened by (i) rarity or lack of associated fossils that might support or oppose the indicated age, (ii) rarity or lack of intervening occurrences of the same assemblage, and (iii) incomplete knowledge of the lineages of the species involved.

In a similar vein, the use of benthonic Foraminifera in paleoecologic interpretation is severely limited by the lack of authentic information about the precise relationships of living species to their environments. Empty shells of Foraminifera, being of small size (0.2 to several millimeters in diameter, in some examples smaller) are rather easily distributed outward as well as moved either upward or downward from their actual living sites. Displacement by gravity, or even by delicate currents, can best be detected by use of a protein test on wet-collected samples. Normally, bottom sediments yield only a minority of living specimens within a matrix including many empty shells of the same forms. Strangers to the living fauna found among these empty shells provide evidence of this sort of dissemination, detection of which is impossible in dry samples. Two examples of the mixing of faunas have been recognized in (i) brackish, estuarine forms occurring in bay facies and (ii) reef forms occurring in lagoon facies; and there are undoubtedly others.

Present and contemplated investigations that will lead toward solutions of the current problems are

1) Search for other kinds of planktonic fossils that give the same answers as the floating Foraminifera.

2) Search for new records of planktonic Foraminifera, especially distinctive planktonic assemblages in datable association with other types of fossils whose position in the standard time scale is believed established.

3) Study of additional occurrences of the already known planktonic assemblages, from submarine dredge-samples, drilled wells, and elevated deposits.

4) Careful study of ontogeny and phylogeny as applied to speciation and lineages, especially among the known or supposed planktonic forms.

5) Study of the floating characteristic at various levels within the oceans, as it applies to species and genera not commonly regarded as planktonic to determine its influence on distribution of the Foraminifera.

6) Study of the benthonic fraction of largely planktonic populations from known depths in Recent seas.

7) Determination of the physical and chemical factors that affect the distribution patterns of living species and possibly affect the evolutionary development of species and genera.

Studies such as these suggested here promise significant help toward more accurate use of fossil Foraminifera, both as facies indicators and in long-range correlation.

RUTH TODD

U.S. Geological Survey
Washington, D.C.

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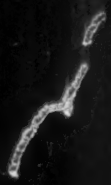

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1. R. S. Adams and C. E. Watson, *J. Biol. Chem.* **147**, 460 (1943).
2. Dicumarol is the trademark for. . . .
3. S. H. Aston, *An Introduction to Biochemistry* (Street & Smith, New York, ed. 3, 1948), p. 36.
4. White's determination of this factor involves. . . .

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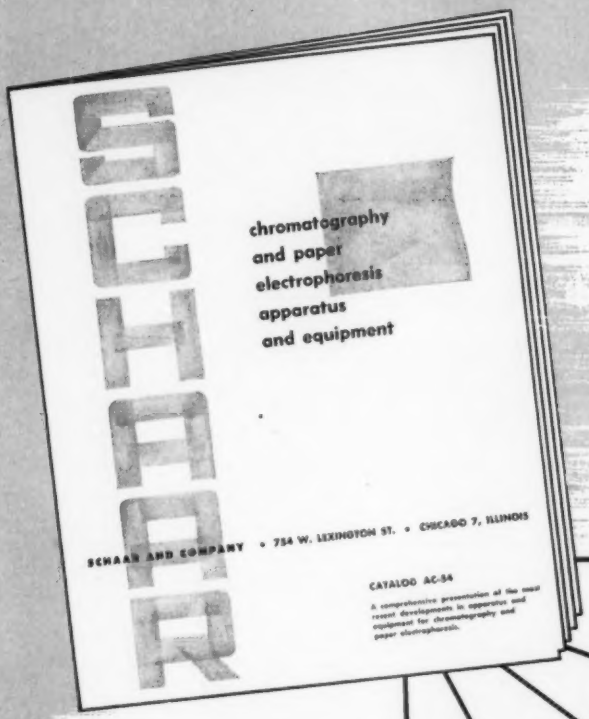

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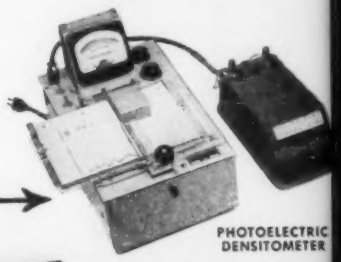

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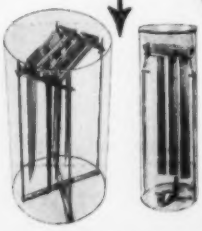

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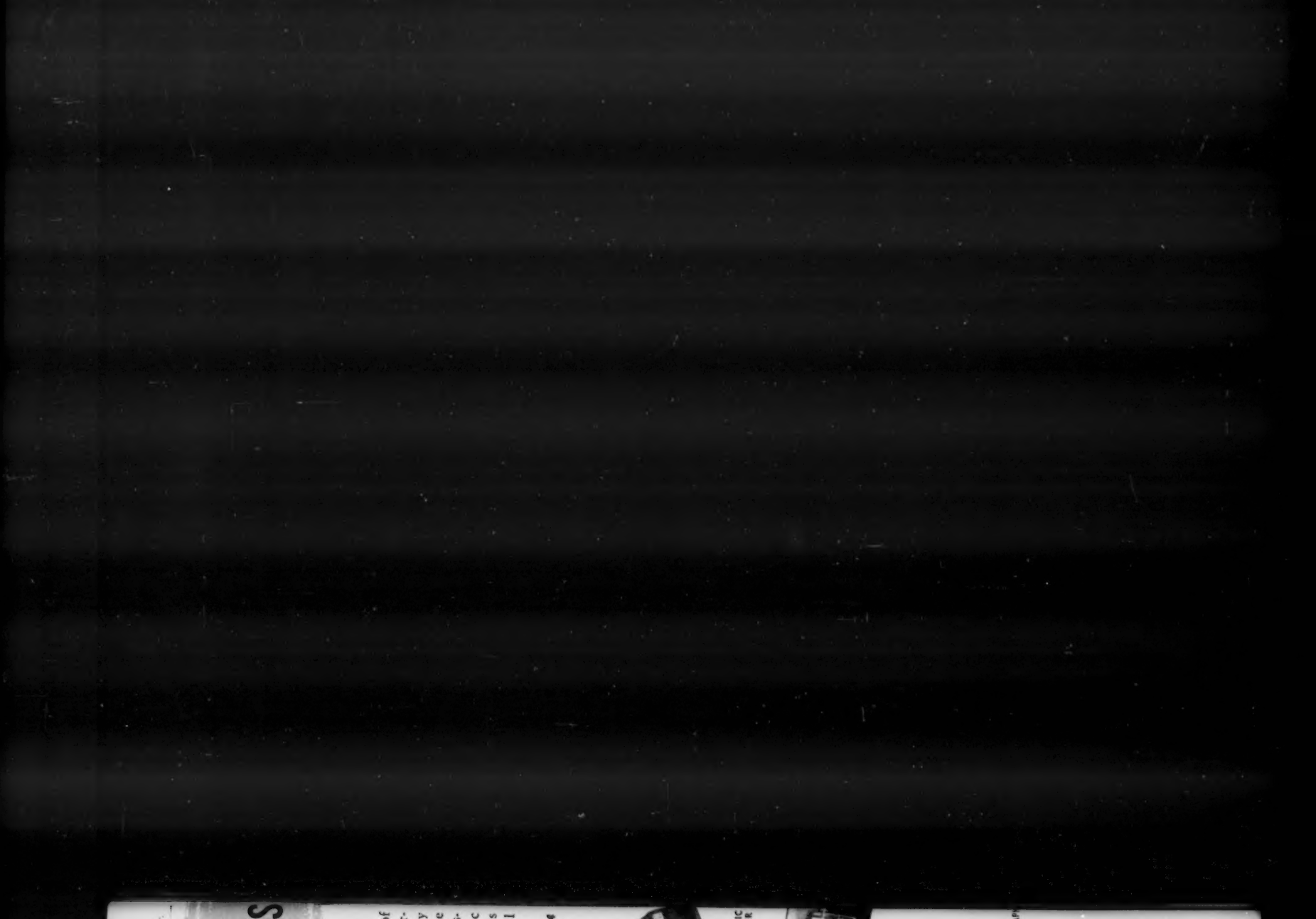

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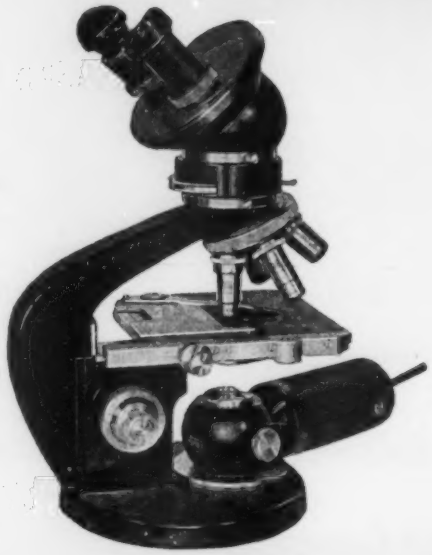

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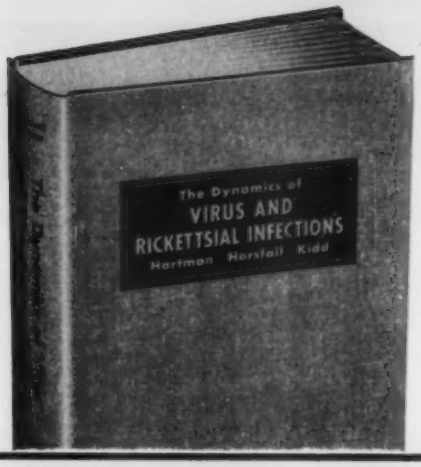

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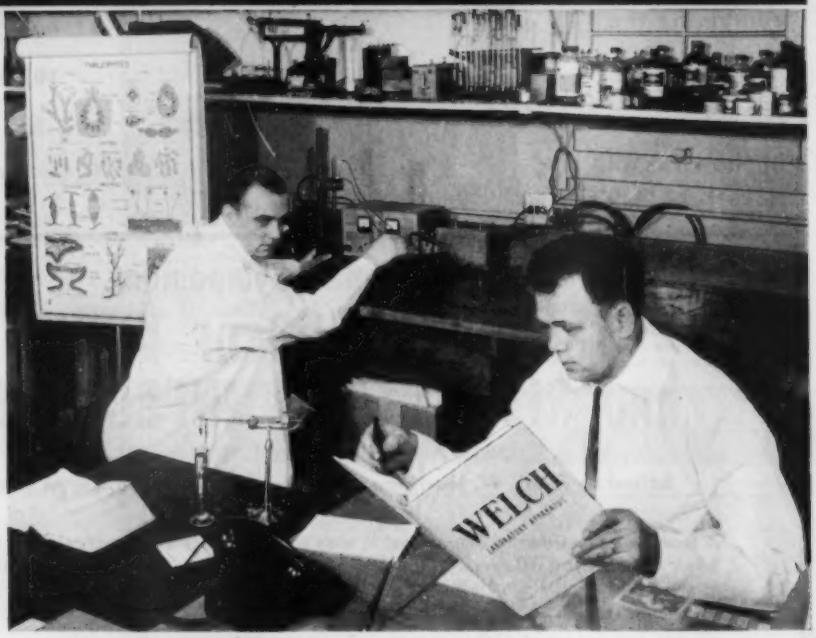

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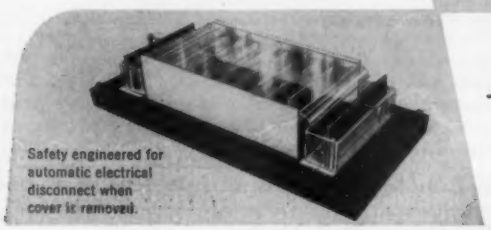

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596 *Contributions to American Anthropology and History.* Vol. XI, Nos. 52-56. 1952. Quarto, v + 236 pp., 1 frontispiece, 145 figs. Paper, $6.75; cloth, $7.50.

Williams, Howel. Geologic Observations of the Ancient Human Footprints near Managua, Nicaragua. Pp. 1–31, 11 figs. (Contr. 52.)

Shook, Edwin M., and Alfred V. Kidder. Mount E-III-3, Kaminaljuyu, Guatemala. Pp. 33–127, 81 figs. (Contr. 53.)

Roys, Ralph L. Conquest Sites and the Subsequent Destruction of Maya Architecture in the Interior of Northern Yucatan. Pp. 129–182, 4 figs. (Contr. 54.)

Strömsvik, Gustav. The Ball Courts at Copan; with Notes on Courts at La Union, Quirigua, San Pedro Pinula, and Asuncion Mita. Pp. 183–214, frontispiece, 23 figs. (Contr. 55.)

Smith, Robert E. Pottery from Chipoc, Alta Verapaz, Guatemala. Pp. 215–236, 26 figs. (Contr. 56.)

600 Burlew, John S., edited by. *Algal Culture: From Laboratory to Pilot Plant.* 1953. Octavo, ix + 357 pp., 92 figs. Paper, $1.25.

601 Wilson, Ralph Elmer. *General Catalogue of Stellar Radial Velocities.* (Papers of the Mount Wilson Observatory, Vol. VIII.) 1953. Quarto, x + 344 pp., Paper, $2.50; cloth, $2.85.

Year Book 52, July 1, 1952–June 30, 1953. Reports on current research from all the departments of the Institution. 1953. Octavo, xxxix + *18* + 309 pp., 7 pls., 29 figs. Paper, $1.00; cloth, $1.50.

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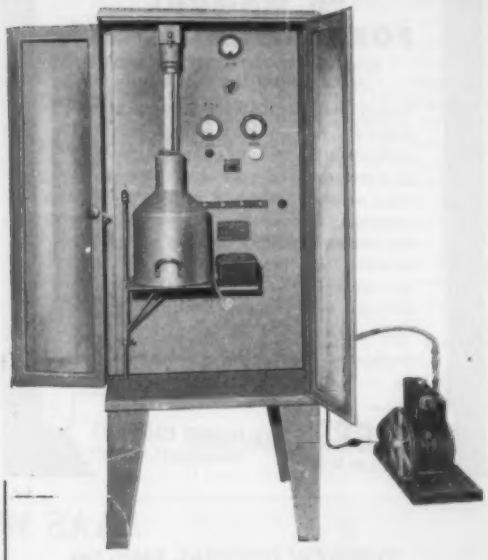

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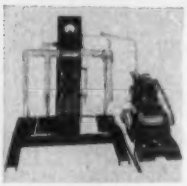

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While UNITRON phase Microscopes are new, this report on them is not. It is a repetition of what was said in the recent Convention issue of Science. The interest shown in that report was so great, and the requests for catalogs so numerous, that we feel it is worth repeating.

Phase microscopy in the news

Our Phase Microscope Exhibit at the AAAS Meeting received an unexpected bit of advance assistance with the announcement in November that Dr. F. Zernike was awarded the 1953 Nobel Prize in physics for his development of the phase microscope. As a result of this announcement, many who attended the Boston Meeting knew more about phase microscopy than would otherwise have been the case. The phase microscope is so relatively new, and the conventional phase instruments so expensive, that real familiarity with this latest development has been largely limited to an inner circle of zoologists for whom the phase microscope is an absolute necessity. This is an unfortunate situation since phase microscopy has an equally wide application in large areas of industrial research, in routine medical and laboratory testing, and in the student laboratory.

Phase microscopy in a nutshell

Briefly stated, the phase microscope permits the examination of thin, transparent specimens whose structural details vary only slightly in thickness, absorption, and refractive index from their surrounding medium. With the ordinary "bright field" microscope, such specimens must be stained in order to introduce contrast and detail. Aside from requiring skill and laborious preparation, staining techniques produce a physical distortion of the object and involve the death of living specimens. For the zoologist the importance of the phase microscope lies in its ability to show activities in the *living* cell.

Busy booth

The microscopes on display in our booth at the AAAS Meeting ranged from UNITRON Student Models to the large UNITRON Universal Camera Microscope. The constant stream of visitors showed greatest interest in trying for themselves the new UNITRON Phase Microscopes. Two microscopes of each model were placed side by side with one instrument functioning as a phase microscope and the other as a conventional bright field type. The *unstained* specimen viewed was the same in both cases—*somatic chromosomes of Trillium kamtschaticum*, if you're interested. Observers were astounded by the difference between the two images. The demonstration was actually *too* successful; the image under bright field was so washed out in appearance that we were frequently challenged to prove that we really had a specimen on the slide. It took but a moment to change the microscope from bright field to phase contrast, and the observer from a state of scepticism to one of admiration.

Phase contrast for the amateur

To those acquainted with the cost of conventional phase microscopes and unacquainted with the new UNITRON Phase Microscopes, it will seem that the word "wealthy" has been omitted from the above section heading. But it's true—we have a *complete* student phase microscope with 3 objectives and 2 eyepieces, magnifying 32-600X, available for as little as $99. We are rather proud of the report on this instrument given by Professor Julian Corrington in the February issue of *Nature Magazine*. In his column, "Under the Microscope", he states:

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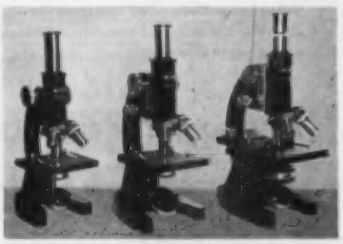

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25–29. American Assoc. for the Advancement of Science, Southwestern Division, Lubbock, Tex. (F. E. E. Germann, Dept. of Chemistry, Univ. of Colorado, Boulder.)

29–30. Eastern States Health Education Conf., New York, N.Y. (I. Galdston, 2 E. 103 St., New York 29.)

29–30. Symposium of Recent Advances in the Study of Venereal Diseases, 6th annual, Washington, D. C. (J. K. Shafer, Public Health Service Division of Venereal Diseases, Washington 25, D. C.)

29–1. American Mathematical Soc., Chicago, Ill. (J. W. T. Youngs, Univ. of Indiana, Bloomington.)

29–1. American Physical Soc., Washington, D. C. (K. K. Darrow, Columbia Univ., New York 27, N. Y.)

29–1. Midwestern Psychological Assoc., Columbus, Ohio. (L. J. Cronbach, 1007 S. Wright, Champaign, Ill.)

30–1. Minnesota Academy of Science, annual, Northfield, Minn. (S. P. Miller, University of Minnesota, Minneapolis.)

30–1. South Dakota Acad. of Science, annual, Rapid City, S. Dak. (A. L. Haines, Chemistry Dept., Univ. of South Dakota, Vermillion.)

May

2–6. Electrochemical Soc., spring, Chicago, Ill. (H. B. Linford, Columbia Univ., New York 27.)

2–7. Soc. of American Bacteriologists, annual, Pittsburgh, Pa. (F. S. Cheever, P.O. Box 1912, Pittsburgh 30.)

3–5. American Geophysical Union, 35th annual, Washington, D.C. (J. Adkins, Office of Naval Research, Washington 25.)

3–6. Air Pollution Control Assoc., Chattanooga, Tenn. (H. C. Ballman, 4400 5 Ave., Pittsburgh 13, Pa.)

3–7. American Psychiatric Assoc., annual, St. Louis, Mo. (R. F. Gayle, Jr., Professional Bldg., Richmond 19, Va.)

3–7. Soc. of Motion Picture and Television Engineers, semiannual, Washington, D.C. (Sec., 342 Madison Ave., New York 17.)

3–8. International Conf. on Complete Gasification of Coal, Liége, Belgium. (J. Venter, 7 Blvd., Frére-Orban, Liége.)

4. World Health Assembly, 7th, Geneva, Switzerland. (WHO, Palais des Nations, Geneva.)

4–6. Electronic Components Symposium, Washington, D.C. (F. B. Haynes, Glenn L. Martin Co., Baltimore 3, Md.)

5–7. American Inst. of Electrical Engineers, northeastern district, Schenectady, N.Y. (H. H. Henline, 33 W. 39 St., New York 8.)

5–7. Forest Products Research Soc., annual, Grand Rapids, Mich. (F. J. Rovsek, Box 2010, University Station, Madison 5, Wis.)

5–8. National Conf. on Health in Colleges, 4th, New York, N.Y. (Sec., American College Health Assoc., 1790 Broadway, New York 19.)

6–8. American Philosophical Assoc., Urbana, Ill. (M. C. Nahm, Bryn Mawr College, Bryn Mawr, Pa.)

7–8. North Carolina Academy of Science, Greenville, N.C. (J. A. Yarbrough, Meredith College, Raleigh.)

8–16. International Cong. of Thalassotherapy, Dubrovnik, Yugoslavia. (C. Plavsic, Zeleni Venac 1, Belgrade, Yugoslavia.)

(See the March 15th issue for summer meeting lists.)

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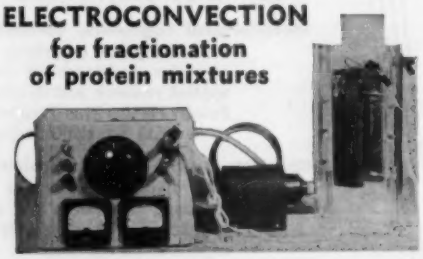

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